PHYSIOLOGY OF DIGESTION

AND THE

DIGESTIVE ORGANS.

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PHYSIOLOGY OF DIGESTION.

LECTURE I.

GENERAL INTRODUCTION.—THE LOSSES OF THE ANIMAL BODY.—THE NATURE OF FOOD.—THE PRINCIPLES OF DIETETICS.

IF we study attentively the living animal body we come to the conclusion that it is continually wasting, and that every vital act is associated with, and necessarily dependent upon, a certain loss of matter. If, for instance, the animal body were placed in one scale of a balance-pan, and its weight determined at one particular moment, if the balance were sensitive enough we should find the next moment that the weights which exactly counterpoised the animal no longer did so.

Let us consider the causes of this loss of weight. I blow through a glass tube into the lime-water contained in this glass, and you observe that the perfectly pellucid and clear lime-water becomes more and more milky; and if I place the glass aside for a few moments, there will fall a deposit consisting of calcium carbonate. This experiment affords the simplest way of showing that one of the sources of loss of the animal body is due to carbonic acid which is continually being evolved by it. I now draw your attention to the bell-jar on the lecture table, below which you observe a living guinea-pig. Arrangements have been made for drawing a stream of air through the bell-jar. In its passage to the bell-jar the air has to bubble through a vessel containing lime-water, and again on its exit from the bell-jar the air bubbles through a second similar piece of apparatus.

Observe that whilst the lime-water in the first vessel is only feebly opalescent, indicating that the air contains but a small quantity of carbonic acid, the lime-water contained in the second vessel is becoming more and more turbid. This experiment is, as you will admit, more satisfactory and more instructive than that of simply blowing through lime-water, for it teaches us that the carbonic acid which is thrown off by the animal body is actually produced within it. We might readily modify the simple respiratory chamber in which the guinea-pig is now placed so as to permit of our determining the *amount* of carbonic acid which is produced by it in any given time. We might for instance pass the whole of the air which leaves the chamber through a weighed receptacle containing some substance such as caustic potash or caustic soda, which possesses the power of absorbing and combining with carbonic acid: such determinations have been made in the case both of the lower animals and of man, and to certain of the results obtained in this way I shall afterwards direct your attention. Now the carbonic acid which has been produced by the body of this guinea-pig and whose presence is attested by the opalescence of the lime-water is thrown off in the greatest part by the respiratory organs, the lungs, and also in some measure by the skin.

Amongst the chief continuous losses of the body is that of watery vapour. Under ordinary circumstances we do not appreciate that no small quantity of water is continuously passing off from our lungs and respiratory passages, together with the carbonic acid. When the temperature of the external air falls very low, the presence of water is, however, rendered perfectly obvious to our senses by its immediate condensation as the breath meets the air, and by the deposition of water upon cold surfaces, as, for example, upon windows of confined and imperfectly ventilated rooms, in which human beings or other living animals are confined.

By again modifying our apparatus we might in the case of this guinea-pig determine the amount of water passing

as watery vapour into the air which traverses the chamber. I shall afterwards have to consider with some degree of care the statistics of the animal body, and to bring before you the actual amounts of the losses which the body daily sustains, but at present, without going into details, I wish to impress upon you the fact that, as it lives the body of necessity loses large quantities of matter, amongst the chief of which are carbonic acid and water. The amounts of these substances are not, I may add, constant quantities, but depend particularly upon the weight of the body, upon the amount of food consumed in a given time, and upon the amount of work done by the body.

Leaving the animal body for the present, let me direct your attention for a moment to the phenomena of combustion. To the bent wire which I hold in my hand I have attached, as you observe, a small wax taper which I light. I plunge the taper into a glass gas-jar with narrow neck standing over water, and we observe that at first the taper burns vividly. As it continues to burn a little water is condensed on the sides of the jar, but now the flame begins to grow fainter. The light evolved diminishes ; and, as I speak, the flame is extinguished, or rather just about to be extinguished, for on rapidly drawing the taper into the air, the yet smouldering wick bursts into a flame again, which is extinguished however completely, if, as you now see me do, I re-plunge the taper into the gas-jar and leave it there. As the taper burned, there has been produced water, which in part is evident to our senses in the dew which has condensed upon the sides of the vessel, and large quantities of carbonic acid, which, like the carbonic acid evolved by breathing animals, is not obvious to us unless we have recourse to some simple chemical method of demonstrating its presence. How much carbonic acid is produced during the combustion of a taper similar to that used in the last experiment, is obvious to all when I pour some lime-water into this stoppered bottle, in which a taper was burned to extinction. The abundant precipitate of calcium carbonate again testifies to the fact which I wish to demonstrate. In the

process of combustion a candle, then, has produced carbonic acid and water, and, as you all see, its substance has diminished. So rapid is the process of combustion in this case that the diminution in the mass of the burning body needs no balance in order that we may detect it.

The process of combustion as it is illustrated by this burning candle consists in an active and rapidly progressing oxidation of the burning body. The latter is in the case of the wax taper composed of organic chemical compounds rich in carbon and hydrogen, and containing but little oxygen. The carbon and hydrogen uniting with the oxygen of the air form carbonic acid and water, and in doing so there is evolved heat so intense as to produce visible light, which is associated with this particular act of combustion. The products of combustion in this case are carbonic acid and water.

The animal body, like the candle, consists in great part of organic chemical compounds. As the animal lives, its substance burns, that is, oxidises. The carbon and the hydrogen of its organic compounds combine with oxygen and give rise to carbonic acid and water. Though the magnitude of its operations may be, and often is, very great, the intensity of the process of combustion at any one moment, is not, however, such as to be rendered obvious to our senses by the evolution of light, although, as I shall afterwards more particularly point out, it is accompanied by the evolution of very much heat. It will serve to impress upon your minds how great is the analogy between the greatest, and if I might so say, final chemical operations of the animal body and the combustion of a candle, if I show you another experiment relating to this division of my subject. Standing in a basin containing water is a gas-jar, having a capacity of about a quart. This gas-jar is fitted with an india-rubber stopper perforated in its centre so as to admit an accurately fitting glass tube to which is attached an india-rubber tube, which I shall afterwards introduce into my mouth. At present the gas-jar contains air having the composition of the air of the room, and, therefore, able to

support animal life and combustion. Were I to place a burning taper in the jar it would, as in the previous experiment, burn for some minutes until the greater part of the oxygen of the air had been removed or replaced by carbonic acid. Placing, however, the elastic tube connected with the gas-jar into my mouth, I now make a forcible inspiration, so as to draw the whole of the air which it contains into my lungs and air passages. Immediately thereafter, by a forced expiration, I expel the water which has been drawn into the jar into the basin, and the jar now contains atmospheric air modified by its passage through the lungs. I now light a taper and plunge it into the jar. You observe that the flame is instantly extinguished, indicating that, in the process of respiration, the air which has passed through the lungs is so modified that it will no longer support the combustion of combustible bodies : that it has been modified in the same manner as it would have been by a combustible body burning until combustion was no longer possible.

It was the great French chemist Lavoisier, who, in the last century, co-ordinating facts which had been ascertained by our countrymen Mayow, Black, Priestley, and others, and adding a great many which he himself had discovered, established the remarkable truth that the process of respiration in animals is essentially the same as the process of combustion. He ascertained that the chief products of respiration of the animal body were identical with the products of combustion of the substances chiefly used as fuel, and he asserted that the heat of the animal body is, like the heat produced in ordinary combustion, due to the chemical union of carbon and hydrogen with oxygen. This great philosopher, however, committed the mistake of localising the combustion of the animal body in the lungs. It was in these organs that he surmised the blood to be heated, and hence the heat of the animal body to be distributed. We now know that the living animal body is everywhere the seat of oxidation processes, which result in the production of carbonic acid and water ; these chemical processes being, however, more intense in those organs in which vital

processes are most active; while the processes which go on in the lungs are recognised as being essentially processes concerned in the interchanges of gases between the air on the one hand, and the blood on the other.

We may therefore say with strict accuracy that the human body from hour to hour is consumed like a candle; the combustion in the candle is rapid and luminous, and occurs only in conditions of high temperature; that of the body is slow, non-luminous, and takes place in the comparatively cool wet tissues; nevertheless they are essentially similar, in that in both cases the combustion is supported at the expense of loss of substance, and at the cost of the oxygen of the air; and in both cases new substances are evolved by the combination of the latter gas with the matter of the burning body.

The points of difference must be sought in the dissimilarity of the substances which are burned. The fatty or waxy matter of the candle is a compound of C, H, and O, which can only yield bodies containing these elements with the O of the air; such are the CO_2, and the H_2O, whose formation during combustion has already been demonstrated. On the other hand, there is no tissue of the human body which does not contain, as essential constituents of their structure, complex nitrogenous bodies. In the muscles, in the glands, in the brain, in the blood, in all the parts which we are accustomed to regard as characteristic of a living body, N is found as a constituent of the very first importance. We are not surprised, then, that N-holding bodies, like the carbonaceous, fall victims to the all-devouring fire of life, and are represented in the class of substances evolved in its combustions. In other words, the body of an animal evolves CO_2, and H_2O, just as does the burning candle; but in addition it evolves a body, or bodies, containing N. Of these urea (CH_4N_2O) may be taken as the type; it is excreted by the kidneys and also to a small extent by the skin.

We are now in a position to inquire more particularly, what are the total losses of an average human body in the course of 24 hours?

It has been estimated that the body loses in 24 hours about 6lbs. of water, and rather over 2lbs. of other matters, of which the chief is carbonic acid. The amount of carbon corresponding to the carbonic acid amounts in 24 hours to 4000 grains. The amount of nitrogen amounts to about 300 grains.

But if a body loses 8lbs. in weight every 24 hours, it is a simple calculation to ascertain how speedily that body would be reduced to nothing. The losses must be daily repaired; new matter must be added to counterbalance that which is lost; and the obvious source of such renewal of substance is the food we eat, and the water we drink. From this consideration there arise important questions: Is it the daily supply of food which is consumed in the body? Is the body, as it were, the lamp and the wick, and the food that we daily eat the oil for the lamp? Does the body really correspond to the candle itself suffering combustion,—or is it not rather the candlestick containing the consuming substance? There is indeed much to be said for this view of the matter suggested by these questions. The well-nourished body of a healthy man contains besides the indispensable components without which existence from moment to moment would be impossible, other tissues rich in stored-up matters for future use. The lamp is furnished with a reservoir of oil enough to feed its flame in the absence of the usual daily replenishing. Such a store in the body is the fat which fills up the hollows of the frame and gives the plump sleekness to those who are, physiologically speaking, well-to-do. But besides this, much substance contained in other parts, even in important and indispensable organs, such for example as the muscles, may be regarded as stored material available for future consumption in case of need. Hence when an animal is deprived of all food it does not at once die—the flame does not forthwith flicker down and expire—but the combustion proceeds, though much reduced in intensity, and the excretory substances are evolved and cast forth as formerly. Meanwhile the matters of the body, lacking

reinforcement, dwindle rapidly, but not equally ; and when the body has been thus reduced in weight by a certain proportion which is almost constant for each kind of animal and each phase of life, death ensues ; the oil has been spent, and there is nothing but the empty lamp remaining.

Of all the tissues of the body, the fat is that which wastes the most quickly during starvation ; it may even disappear entirely. The liver, which also is a large storehouse for the rest of the body, yields up its store completely. The muscles, except that of the heart, supply fuel to the struggling flame ; and even the blood loses much of its substance. The brain and spinal cord alone preserve their weight during complete starvation, and seem to have no portion that can be made to serve as fuel for the body at large.

We see, then, that so long as life continues, whether food be taken or not, the body, moment by moment, loses weight ; when loss ceases, life ceases. But loss of weight is not the only loss the body momently suffers. In addition to loss of substance, there is a continuous loss of energy.

The Energy of the Body.

Thanks to the lucid expositions of many brilliant teachers, the popular mind is beginning to attach clear notions to this term *energy*. Nevertheless, some illustration of its meaning in connection with the life of our body, may not seem superfluous. *Energy*, in the technical sense in which I use it here, may be translated into *the power of doing work :* and the loss of such power of doing work seems to be as inseparably associated with our conception of living matter as the loss of substance has been shown to be. How may loss of energy be exhibited by a body ? If I were to take a large solid iron ball and heat it in a furnace to redness, and suspend it by a chain from the ceiling of a lofty room, the ball would sooner or later grow cold : it would give up its heat to the bodies or the space surrounding it—in other words, it would *lose* heat. But at the same time, and in the same degree, it would lose the power of

doing work. The power which a red-hot cannon-ball possesses of doing work, is one which may be readily demonstrated. If such a ball be plunged into a cauldron of cold water, the energy (*power of doing work*) which is continually streaming from all parts of its surface is caught up by the water, and might be utilised by a simple apparatus to do the work of a steam engine. When the ball is cold once more, this power of doing work is gone.

Take another example. When I wind my watch up at night, I impart to the coiled spring a certain quantity of energy—of power of doing work—which slowly dribbles away at every click in the ceaseless motion of the wheels. In 24 or 36 hours the watch has lost all its power of doing work—its energy has escaped from it. If by chance the main-spring snaps, suddenly the whole energy escapes in a second or two, with the well-known whirring of such a disaster. Again, a charge of gunpowder, or a charge of dynamite, in the interior of a bomb, possesses an enormous power of doing work. Such energy might conceivably be allowed by a proper mechanism to escape little by little, in a somehow useful manner: we all know, however, with what destructive violence such a body commonly parts with its stored-up power of doing work.

I may at once point out a distinction which it is convenient to draw. If I wind up a clock, much energy or power of doing work becomes latent in the spring. If I omit to set the pendulum swinging, the energy remains latent for an indefinite time: the clock possesses the potentiality of doing work; its energy is *potential*. When the pendulum begins to swing, the "escapement" allows the pent-up steel to unroll itself gradually bit by bit: work is done, the power of doing work is operative, the energy is *actual* or *kinetic*. All energy belongs to one or other of these two classes. The energy of the red-hot ball is actual; that of the explosive before ignition is potential.

Now a living body, say of a man, as has been said, is as continuously losing energy as it is losing matter and weight. We observe this in many ways. In the first

place, the body is the seat of movements, some of which are voluntary and others involuntary. The being whom we are studying may, in virtue of the contraction of his muscles, perform work which we may estimate. The amount of work done in a working day of 24 hours may actually amount to 150,000 kilogramme metres, that is to as much work as would be required to lift nearly 480 tons to the height of one foot. But assuming that the human being which we are studying is not exerting any voluntary muscular effort or doing any external work, we may yet observe that it is the seat of movements which are unceasing, and whose continuance is absolutely essential to life. The movements of respiration and the contractions of the heart are the most obvious of these.

If our study be an exact and not a superficial one, we shall come to the conclusion that the marvellous pump, the heart, which is ceaselessly engaged in driving blood throughout the body, is performing an amount of work which might be estimated without exaggeration as at least equal in 24 hours to the work expended in lifting 120 tons to the height of one foot, while almost certainly it would greatly exceed this estimate, that is to say, that the heart of a person who is almost absolutely at rest does an amount of work which is a sensible fraction of the *external*, or, to use a popular expression, the *manual* labour performed in the working day of a hard-working labourer.

Next to the movements voluntary and involuntary which we are just considering, the heat of the animal body attracts our attention. If with a thermometer we observe its temperature, we are made aware of the marvellous fact that so long as it is in a state of health the temperature of the body is nearly constant, and that the temperature is very much above that of the medium which surrounds the body, varying between 98° and 100°. If we plunge the body under observation into a cold bath surrounded by non-conducting materials, or if instead of plunging the whole body we simply experiment upon a part of the body, for example one of the lower extremities, we ascertain that

by contact with the body the water becomes heated, and if we determine the amount of water raised in temperature, and the amount of the increment of temperature, we obtain an estimate of the loss of heat sustained by the body. We may thus determine that the human body under observation loses in 24 hours an amount of heat which corresponds to that required to raise, say 2839 kilogrammes of water one degree Cent., or, in other words, to raise about 62 pounds of water from freezing point to boiling point. If we appeal to the experience of the physician and to the experience of mankind, we are told, too, that this normal temperature of the animal body is a necessity for its continued existence, and that were the temperature of the body to be permanently lowered to any considerable degree, the functions which are most essentially vital, that is, most necessary to the continuance of life, cease, and death ensues.

We now approach the question of the source wherein our store of matter and of energy in the body is continually replenished. *Ex nihilo nihil fit:* a body which continually loses substance and yet maintains its weight, and a body which, while continuously losing energy, yet retains its power of doing work, must depend upon the introduction of new matter and new energy from without.

The substances lost are retrieved, as must be obvious to the simplest child, in the food which is eaten : it is equally true, although not so obvious, that the lost energy is recovered from the same source. In short, the substances which enter the body have not the same form as the substances which leave it : starch, albuminous matter, fatty matter, are introduced as food ; but carbonic dioxide, water urea, are the representatives of these substances in the excretions. Similarly the energy which enters the body is (with trifling exceptions) unlike that which escapes : in the former case it is *potential*, in the latter it is *actual* or *kinetic*. And these two concurrent series of events, viz. the transformation of matter on the one hand, and of energy on the other, are inseparably associated. Matters are introduced into the body in one chemical form and

while there are converted into other and more stable forms: and in the course of this transmutation actual energy of heat and mechanical movement appears and escapes. If you ask me what is the general nature of these chemical changes out of which so much energy appears which before was latent or potential, I can refer to that cardinal comparison with which I started, viz. the comparison of the living body to a burning lamp, and tell you that the chemical changes which are linked at every step to the manifestations of life are oxidations of a more or less evident kind.

Here, then, we have the explanation of the continuous wasting and renewal of the body: there is no life (in our physiological experience of it) without the conversion of potential into actual energy: there is no such conversion without the chemical transmutation of unoxidised or partially oxidised matters into matters more perfectly oxidised: there can be no such oxidation without the continual renewal of the factors of it, and the continual removal of the effete substances.

Whilst certain of the losses of the body are absolutely continuous, to wit the loss of carbonic acid and a portion of its water, other of its losses are, as it were, intermittent, these matters being accumulated in proper receptacles and then thrown out of the economy.

Like the losses, the gains of the matter of the body are in part continuous, in part intermittent. For instance, the body is without ceasing receiving oxygen gas which in the case of air-breathing animals is derived from the atmosphere which they breathe, and in the case of aquatic animals from the air dissolved in the water which they inhabit, the oxygen which is being continuously received by the body being very nearly, though not exactly, equal in amount to the carbonic acid which is being simultaneously expelled by the process of respiration.

The intermittent sources of gain of the animal body are constituted by the food and drink which from time to time are introduced into it. Of all the constituents introduced

in this way, by far the most abundant is water, which constitutes not only the greatest part of the liquid, but which is also present in considerable proportion in all those solid articles of food which we consume. Besides water, the food contains certain mineral constituents, amongst which may be mentioned as most abundant common salt, whose presence in and passage through the animal body and its various tissues and organs, appears to be absolutely essential to a variety of the chemical and especially physical processes which have their seat in these. The solid constituents of food contain, however, as their principal constituents certain organic bodies belonging to few perfectly defined groups, and which are of such a nature that they or their derivatives may in great part be so acted upon as to enter into and become as it were part and parcel of the various tissues and organs; in other words, be *assimilated*.

There are, it will be observed, very close analogies between the animal and such a piece of mechanism as the steam engine. Thus the energy at the disposal of both is primarily derived from the oxidation of combustible matters. Again the potential energy latent in the combustible matters and the oxygen to which as yet it has no suitable access, appears as heat and mechanical movement chiefly. Some of the most salient points of difference must, however, not be lost sight of:

(1) The waste of the essential parts of such a machine as the steam engine is insignificant, and bears no definite relation to the work done; the kinetic energy of the machine is primarily due to oxidation processes taking place in the furnace, and in no respect to changes in the substance of the machine. The animal on the other hand wastes continuously in all its parts and organs, and its energy is derived immediately from material which has become part and parcel of the various mechanisms.

(2) Any substance capable of being readily oxidised (burned) and thus of generating heat may be used as fuel in the steam engine, provided its oxidation admits of being

conducted with safety to its furnace, whilst the substances which can form the food of animals belong to few groups which include but a comparatively small number of bodies. The constituents of food have not only to supply energy to the body but they must further be capable of prior conversion into the very substance of the animal body, into its very "flesh and blood." Moreover the constituents of food must be very free from traces of the peculiar substances which we term poisons, and which by their presence have the power of impairing and stopping the action of various organs of the body, and in this way terminating life.

Let us now return to consider what are the losses of the matters of the body in 24 hours. An average human body loses in 24 hours of water about 40,000 grains or 6lbs.: of other matters about 14,500 grains, or over 2lbs. The latter contains carbon, mostly in the form of carbonic acid amounting to 4000 grains, and nitrogen excreted mainly in the form of urea amounting to 300 grains; the ratio which the nitrogen bears to the carbon excreted, namely 300 to 4000, or roughly 1 to 13, is a number which I would ask you to remember. The table to which I now direct your attention illustrates the channels through which the water, the nitrogen, and the carbon, are severally excreted.

——	Water.	Other matters.	N.	C.
	grs.	grs.	grs.	grs.
Lungs	5·oco	12·000	..	3·300
Kidneys	23·000	1·000	250	140
Skin	10·000	700	10	100
Fæces	2·000	800	40	460
Total .	40·000	14·500	300	4·coo

Now in order to make up for this loss the body must daily receive about 8000 grains of solid dry water-free food, about 36,500 grains of water, and about 10,000 grains of oxygen, the latter being introduced into the body in the process of respiration.

The Food of the Animal Body the source of its Energy.

We have now to consider more particularly than we have yet done the nature of the solid food which the body requires. In the first instance this solid food, in order conveniently to support the body, should contain the elements carbon and nitrogen in approximately the same proportion as these elements are contained in the matters excreted by the body. In the second place, as has been already stated, these elements must be contained in chemical compounds belonging to a few tolerably well-defined groups.

The organic matters of the foods may be divided into nitrogenous and non-nitrogenous. The former containing the elements carbon, hydrogen, nitrogen, sulphur and oxygen. The latter only the elements carbon, hydrogen and oxygen. All these organic matters, whether they be nitrogenous or non-nitrogenous, are primarily derived from the vegetable kingdom.

The Plant in reference to the Animal.

The plant is the necessary and constant precursor of the animal. The plant organism possesses synthetic powers of a remarkable kind, that is to say, powers of building up out of very simple bodies compounds of great complexity. The plant possesses namely the power, out of carbonic acid, water, ammonia, and a few mineral salts, of building up such complex bodies as vegetable albumins, starches, sugars and fats, the first being nitrogenous, the second and the third being non-nitrogenous.

When we inquire further into the nature of the processes which go on in the vegetable organism we find that these processes of synthesis or building up are intimately connected with the power which the plant possesses of separating the atoms of certain chemical compounds presented to it, and building up the separated atoms into new combinations. Such a body as starch for instance necessitates on the part

of the plant a separation, a tearing asunder, as it were, of atoms of carbon from atoms of oxygen as they existed in carbonic acid, the carbon being retained by the plant-cell, while the oxygen is in part thrown out of it.

This remarkable power of tearing asunder the atoms existing in the simple bodies which constitute the chief elements of plant food, is however only possessed by the plant in the presence of the rays of sunlight. It is the radiant energy of the sun which, acting through the intermediation of the vegetable cell, tears asunder carbon from oxygen, hydrogen from oxygen ; and the energy which has effected the decomposition becomes, as it were, latent in or associated with the separated atoms in the position which they occupy in the newly formed complex organic bodies. All the bodies thus formed, *the proteids*, *the starches*, *the sugars* and *the fats*, are combustible, that is to say under favourable circumstances they may be made to oxidise or burn, and in the process of oxidation or combustion the *potential* energy which was stored in them becomes *actual* or *kinetic*, and takes the form of heat. All these substances may similarly be used as articles of food for animals and be burned within the tissues, and thus furnish the animal with the energy which it requires for the performance of the external work which the individual has to perform, and for the maintenance of the temperature which is so necessary to the life of the body. Some of my hearers may be surprised at the statement that organic constituents contained in the food of the animal body are derived entirely from the vegetable kingdom, and may remark that man partakes of food which in great measure is derived from animals, and not from plants. I would point out to these, however, that the animals which we consume as food, or the milk which is supplied to us by certain of these animals, furnish us with matters derived primarily from the vegetable kingdom, and which have been in some degree modified, and yet substantially stored up for our use by the animal. The sheep and oxen whose flesh we consume are but store-houses containing plant products which these creatures accumulate in

their tissues for our use, so that when we consume the flesh of an ox, though we obtain the proteid which that flesh contains immediately from the animal tissue, it is yet but proteid derived in the first instance from plants. As however the diet fit for the support of animal life must of necessity contain an admixture of the various groups of food constituents to which reference has already been made, it is advisable that we should for a moment or two consider the characters of each group.

Classification of the Organic Constituents of Food.

1. *The proteid or albuminous substances.*—The most essential of all the chemical constituents of the tissues of animals and vegetables are called proteid or albuminous bodies.

The animal organism, for instance, in its earliest stage is represented by a single cell, the ovum, which is a nucleated mass of so called *protoplasm.* This protoplasm, matter endowed with marvellous potentiality, contains as its chief constituent the proteid or albuminous bodies which we are now considering. From this one primary protoplasmic mass all the tissues and organs of the body are derived, and in every case descendants of the original protoplasmic mass form the foundation or, as it were, the sub-stratum of the tissues and organs.

The elements carbon, hydrogen, oxygen, nitrogen and sulphur, which proteids contain, are combined together in proportions which differ but slightly in the case of the several proteids.

The following table indicates approximately the variation in the composition of the animal and vegetable proteids:—

	C.	H.	N.	S.	O.
From .	51·5	6·9	15·2	0·3	20·9
To. .	54·5	7·3	17·0	2·0	23·5

In addition to these constituents, the proteids, however carefully they may have been prepared, usually contain a small quantity of mineral matter, the composition of which varies in different cases, chlorides and phosphates of the alkaline metals being the predominant constituents. These proteids, or as they are often called *albuminous substances*, are abundant in blood, in muscles, in milk, in eggs, and are present in considerable proportions also in such vegetable products as wheaten flour or the leguminous seeds. Certain of these proteids are capable of existing in solution in pure water, others only in water holding small quantities of mineral matters in solution, whilst some are altogether insoluble in water. Even those which are soluble in water may be rendered insoluble by sundry agents. The various albuminous bodies present chemical reactions of which some are common to all members of the group, and others more or less characteristic of individual substances. It will be observed that in these bodies the proportion of nitrogen to carbon is very much higher than the ratio in which the nitrogen thrown off from the animal body stands to the carbon.

2. *Starches and sugars.*—These bodies are often spoken of as belonging to the group carbohydrates, an antiquated term which, whilst it has lost its former meaning, may serve to remind us that these bodies contain hydrogen and oxygen in the proportion in which these elements are contained in water, so that the carbohydrates may, so far as elementary composition is concerned, be considered to be made up of a certain number of atoms of unoxidised carbon, and a certain number of molecules of water. The starches and sugars are present in the largest quantities in the vegetable foods which animals consume, though sugar is contained in considerable quantity in milk. The starches are bodies which are generally introduced into the animal economy in an insoluble condition; they will be studied in detail in a subsequent lecture. The sugars are highly soluble bodies. These carbohydrates are usually found associated with proteid matters in various forms of

vegetable food, though the proportion of the two groups varies remarkably.

Thus in peas we have an instance of a vegetable containing large quantities of proteids in reference to starches, while in rice the starches enormously preponderate.

3. *The fats.*—Both vegetable and animal tissues contain varying proportions of fats. The vegetable oils, milk, butter, the adipose tissue of animals, all contain large quantities of fats. Like the starches and sugars, the fats are non-nitrogenous. They contain less oxygen than would be required to combine with their hydrogen to form water. The number of animal fats which preponderate are three so-called neutral fats, termed stearin, palmitin and olein, The first of these is most abundant in the most solid fats, the third in the most diffluent or softest fats. Each of these constituents, namely, olein, palmitin and stearin, may readily be decomposed into the soluble substance glycerine and into a fatty acid : this may be brought about by subjecting them to the action of steam or by boiling them for a considerable time with alkalies or their carbonates. Thus stearin may be decomposed into stearic acid and glycerine : palmitin into palmitic acid and glycerine, and olein into oleic acid and glycerine. Of the fats it may be remarked that they are not, like the proteids, formed only by the agency of vegetable bodies. The animal economy appears unquestionably to possess the power of decomposing proteids, and obtaining from them fats ; and it has also in all probability the power of forming fats out of starches and sugars.

Rationale of a Mixed Diet.

If we now contrast the ultimate chemical composition of proteids, carbohydrates and fats, taking as an example of the proteid group vegetable albumin, of the carbohydrate group starch, and of the fatty group olein, we arrive at the following conclusions :—That the fat contains a much larger proportionate quantity of carbon than either the proteid or the carbohydrate, that its proportionate quantity of

hydrogen is also very much higher, and that the relative amount of oxygen is very much less in fat than in the proteid or the carbohydrate; in this respect the carbohydrate occupies a middle position.

But the most remarkable fact which would be discovered in this comparison would be that the element nitrogen, along with sulphur in smaller proportions, is absent from the starch and the fat, and present only in the proteid group of food-stuffs. As nitrogen is the characteristic and indispensable element in all living matters, the proteid group of food-materials, because it alone contains this element, must be declared to be the essential constituent of all diets. As we survey the tables of elementary composition of the typical constituents of food we gain an insight into the meaning of the instinct which has led man to select a mixed diet, in which proteid, carbohydrate and fatty elements are represented, and in which the two latter preponderate over the former. A man must, as we have pointed out, obtain in his food as much nitrogen as corresponds with that which leaves his body daily in the form of urea, an amount which ordinarily may be set down as about 300 grains. This nitrogen can only be present in bodies belonging to the group of proteids or their immediate derivatives. All diet therefore in order to support life must include proteid or albuminous substances containing at least the above quantity of nitrogen: that is an amount of proteids amounting to about 2000 grains.

But the body requires, besides 300 grains of nitrogen, about 4000 grains of carbon. Were this carbon to be obtained exclusively from proteids, the quantity which would have to be consumed would be enormous; and there would be introduced into the system an amount of nitrogenous material greatly in excess of the requirements.

This would throw an unnecessary amount of work upon various organs of the body, and, as these organs are constituted, would soon lead to disease of them. Instinct however teaches us to mix with the proteid food large quantities of non-nitrogenous food from which the

body may obtain the greater part of the carbon and the hydrogen which correspond to the quantities of these elements which are oxidised.

Calorimetrical value of foods.

Before giving instances of diets which contain the various groups of food constituents in proper proportions to support the life of man, I may add some additional theoretical considerations in reference to the value of the different groups of food constituents as givers of energy to the body. By completely oxidising the same weight of different food constituents in instruments called *calorimeters*, in which the heat of the burned body is employed in heating a known volume of water, or in melting ice, the total amount of energy which each substance is capable of yielding on oxidation may be determined and may be expressed in so-called *heat units*. The heat units employed in such determinations vary, though one may be readily converted into the other; that which is most frequently employed by scientific men is called the *gramme unit* or *calorie*, which may be defined as the amount of heat required to raise the temperature of one gramme of water one degree Centigrade. The table to which I now draw your attention exhibits the number of heat units evolved by the complete combustion of an equal quantity (namely one gramme or 15·432 English grains) of various substances.

Heat evolved during the complete combustion of one gramme of the following substances:—

Albumen	4998
Butter (in its ordinary moist condition)	7264
Fat of ox	9069
Arrowroot	3912
Cane sugar	3348
Urea	2206

These numbers allow us to see at a glance that of all food-stuffs the fatty bodies are those which contain the largest store of available energy. Next to them come the proteids, and lastly the carbohydrates. It would be a

mistake, however, to read such a table absolutely and without reservation. In the calorimeter the substances submitted to experiment are oxidised as completely as it is possible for them to be, and the numbers in the table express the utmost possible yield of energy, supposing oxidation to be carried to its extreme limit. Now the body has not the power of bringing about this perfect oxidation of all substances: some substances are doubtless burnt up into the most stable and ultimate form of CO_2 and H_2O. But such complete oxidation is not possible in the case of proteids, which in all probability are capable of yielding in the body no more than 4263 calories per gramme weight instead of 4998 as stated in the table.

As the object of taking food is twofold—viz. (1) to repair certain losses which the organs and tissues (proteid for the main part) are continually sustaining; and (2) to furnish the body with a sufficient quantity of potential energy—it is obvious that when the body has obtained as much proteid food, together with water and mineral constituents, as will serve to make up the waste of these constituents, it is at liberty to derive from fats and carbohydrates the greater part of the energy it still stands in need of: especially as the oxidation of these latter bodies is very readily accomplished without entailing the excessive labour in certain organs which the combustion of proteid matters would do.

Constitution of an 'Adequate' Diet.

We may now consider an estimate made by the German physiologist Ranke of the various quantities of proteids, fats and carbohydrates which, when present in a digestible diet, are sufficient to support the life of man. According to Ranke a sufficient diet should contain

about	1543	grains	of	proteids,
,,	1543	,,	,,	fats,
and	3703	,,	,,	carbohydrates.

The amount of energy associated with each of those

groups of food constituents is shown in the table which I now bring before your notice.

1543	grains of albumin	give	426,300	calories	
1543	„ „ fat	„	906,900	„	
3703	„ „ starch	„	938,880	„	
		Total	2,272,080		

We have here the amount of various food constituents supplying the body with matter and energy in quantity sufficient, according to Ranke, to make up for the losses under both heads. This estimate is, however, rather too low a one. We are inclined to place more reliance upon the estimates of Forster and Voit, according to whom the following quantities of the chief organic food constituents are required by an average man.

Albumin	118	grammes equal to	1820	grains
Fats	88·4	„ „ „	1364	„
Carbohydrates	392·3	„ „ „	6053	„

The quantity of nitrogen and carbon in the above diet is the following :—

Nitrogen	18·3	grammes equal to	282·40	grains
Carbon	328	„ „ „	5061	„

The value of a diet containing this amount of the various constituents in energy is as follows :—

118	grammes of albumin	give	503,034	calories
88·4	„ „ fat	„	801,699	„
392·3	„ „ carbohydrates	„	1,534,600	„
		Total	2,839,333	calories.

It may interest you to know how much of various articles of food must be consumed in order to supply the organism with the quantity of carbon and of nitrogen which the estimate of Forster and Voit demands. I draw your attention to a table in which on the left hand we have the quantities of various articles of food which contain 18·3 grammes of nitrogen and on the right hand the quantities

of the same articles of food which contain 328 grammes of carbon.

18·3 grammes of nitrogen =			328 grammes of carbon =		
Cheese . .	272 grammes		Bacon . .	450 grammes	
Lean meat .	538	,,	Wheaten flour	824	,,
Wheaten flour	796	,,	Rice . . .	896	,,
Eggs (18) .	905	,,	Cheese . .	1,160	,,
Black bread .	989	,,	Black bread	1,346	,,
Rice . . .	1,868	,,	Eggs (43) .	2,231	,,
Milk . . .	2,905	,,	Lean meat .	2,620	,,
Potatoes . .	4,575	,,	Potatoes. .	3,124	,,
Bacon . .	4,796	,,	Milk . . .	4,652	,,
Beer . . .	17,000	,,	Beer . . .	13,160	,,

This useful and suggestive table indicates to us how very limited are the substances which by themselves will supply the body with the proper quantities which it requires of nitrogen and of carbon, and the same remark applies to the energy which it yields. Thus whilst 538 grammes of meat are sufficient to supply all the proteid which the body requires, if meat alone composed the diet of an animal there would be needed as much as 2620 grammes to supply all the carbon required; but no man could day after day consume such an enormous quantity of meat. Even milk, which contains all the various groups of food constituents, is not adapted to supply all the elements of a perfect diet in their proper proportions for an adult animal; for whilst all the nitrogen which its body needs could be afforded by the consumption of 2905 grammes of milk, in order that the amount of carbon needed should be obtained, the milk consumed would have to reach the enormous amount of 4652 grammes, in other words over ten English pounds.

It will be observed that there is only one article of diet in each of these tables, namely black bread, which contains nitrogen and carbon in such proportions that a moderate weight of it is able to supply the wants of the economy for both these elements. From 1300 to 1400 grammes of black bread constitute, therefore, almost a standard diet, and I may mention that upon this diet large numbers of

men are able to live in health and to accomplish great labours. In some of the departments in the south of France black bread constitutes almost the only food of a vigorous and laborious population.

The Principal Food-stuffs examined.

Although food will be considered in detail in a hand-book specially devoted to the subject, it will be advisable that we should here make some further remarks upon the chief articles of food which enter into the composition of our dietary. We may do so under the following heads.

1. Meat.
2. Eggs.
3. Milk.
4. Vegetable foods.
5. Water and mineral salts.
6. Infusion of tea, coffee and cocoa.
7. Wines, beer and spirits.

1. *Meat.*—Meat is composed of the flesh or muscular tissue of herbivorous animals. In addition to muscular fibres it contains a certain amount of connective tissue with imbedded fat, the latter varying in amount between 4 and 5 per cent. The muscular substance which constitutes meat proper contains about one fourth of its weight of water-free solids, that is to say about 25 per cent. and of this 18 per cent. consists of albuminous substances proper, and about 2 per cent. of gelatigenous substances. When meat is chopped up and treated with cold water, or still better with water heated to about 55 or 60 degrees Centigrade, the water extracts from it firstly proteids, which are almost entirely coagulated on subsequently boiling the liquid; secondly a mixture of nitrogenous so-called extractive matters, of which the chief is a body called creatine; thirdly salts, of which those of potassium are much the most abundant. When meat is treated for a long time with boiling water or water approaching the boiling temperature, in addition the whole of the salts and extractive matters, the so n contains no inconsiderable

quantity of gelatine, formed by the action of water upon the interstitial connective tissue of the meat. Beef-tea is but a solution of the saline and extractive matters of beef; Liebig's extract is but an evaporated beef-tea containing in a small volume the extractive matters and the salts of a large quantity of beef, and in virtue of this possesses medicinal and dietetic properties not to be despised; yet if considered as a food, it in no sense represents the meat which has yielded it, since it has lost the essential albuminous element.

When meat is boiled or roasted the exterior should be rapidly heated, so that the proteids on the surface may at once be coagulated and form a case to prevent the escape of the interior juices. The subsequent cooking may then be carried on at a low temperature—say 160° F.—and with slowness, so as to cause the fibres to set loosely without shrinking or hardening.

The object of the various methods of cooking meat are, if we leave out of consideration the altogether secondary object of rendering it more savoury and appetising, to increase its digestibility and to destroy parasites and the germs of both vegetable and mineral organisms whose subsequent development might be fraught with danger to life.

2. *Eggs.*—An average hen's egg is said to weigh about 1·75 ounce, of which the shell forms one tenth. Eggs contain about 73 per cent. of water, about 15 of albumin, and 12 of fat containing a body called lecithin. The fat and lecithin are mainly contained in the yolk, whilst the greater part of the albumin is contained in the white of the egg. When eggs are boiled the albuminous constituents are, in the case of soft-boiled eggs, heated and only partially coagulated: in the case of hard-boiled eggs, the albumin of the white of the egg and the so-called vitellin of the yolk are coagulated so as to convert them into solid masses.

3. *Milk.*—This liquid, which is the secretion of the mammary gland, constitutes for the earlier part of life, a typical diet, containing representatives of the different

groups of food constituents, although not in the proportions in which these are most useful for an healthy adult body. Milk has a specific gravity which may be as a rule stated at between 1030 and 1033. It contains about 12 per cent. of solids, including about 3 per cent. of fats in the form of butter, about 3 per cent. of casein, about 4 or 5 per cent. of sugar, and about 0·02 per cent. of salts. The sugar which is contained in milk, and which is sometimes called lactose, has a composition $C_6 H_{12} O_6$. *Buttermilk* consists of milk from which the fat has been removed, and therefore contains chiefly sugar, casein, and salts. *Whey* consists of milk from which the casein has been precipitated by the action of rennet. *Cheese* consists of the casein of milk precipitated by rennet: it contains also very much of the fatty matter of the original milk.

4. *Vegetable foods.*—The most important of the articles of vegetable food is *wheaten flour*, which contains about 13 per cent. of a mixture of proteids constituting the so-called *gluten*, and about 73 per cent. of *starch*. Bread is made by mixing wheat-flour with water and salt, so as to form dough, to which is afterwards added yeast. The starch is converted into various so-called dextrins, and then into sugars, which then undergo alcoholic fermentation under the influence of the yeast plant. This leads to the evolution of carbon dioxide, which causes the dough to "rise." When the dough, after being divided into masses of size suitable to form loaves, is heated in the oven to the temperature of 150 or 200 degrees Centigrade, the carbon dioxide and alcohol generated in the process of fermentation are expelled, and in their escape cause the dough to assume a spongy texture and to become "light." Barley and oatmeal, although serviceable as foods, and containing considerable quantities of proteids, do not yield a dough which admits of being made into bread. The value of *oatmeal* as an article of diet is however very well known and recognised by all.

Peas and *beans* afford examples of vegetable foods which are remarkably rich in proteids, containing about 25 per

cent. of legumin, which is closely allied to the casein of milk. They also contain about 38 per cent. of starch.

Potatoes contain on an average about 75 per cent. of water. The solid matter consists mainly of starch with a small quantity of proteid matter and mineral matters which are specially rich in potassium salts.

Fruits and *succulent vegetables* are of value owing to the sugar, the organic acids, and the salts which they contain.

5. *Water and mineral salts.*—The body of man contains more than one half its weight of water, and, as I have told you, very large quantities of water are daily being excreted from the body. Want of water makes itself more imperatively felt, and leads more rapidly to death, than even want of solid food. As, however, the food of man—I refer to the solid food—all contains large quantities of water, life may be supported when but little actual liquid is consumed. The quantity of water, pure or mixed with organic matters, such as alcohol, or coffee and tea-extractives, which is sufficient for a man under ordinary circumstances, may be stated at from one to three pints, though the quantity needed is remarkably influenced by certain circumstances and particularly by the temperature to which the body is subjected.

The mineral matters required daily by man are contained in the various articles of food which he consumes. Instinct, however, leads man to mix with his food considerable quantities of sodium chloride or common salt.

6. *Infusion of tea, coffee and cocoa.*—Tea leaves and coffee berries contain rather less than 2 per cent. of a neutral nitrogenous principle termed *thein* or *caffein.* Tea leaves contain, in addition, large quantities of tannic acid and other extractive matters, amongst which are to be mentioned indefinite and imperfectly known volatile principles to which the infusion owes much of its aroma and taste. Coffee berries contain, in addition to caffein, large quantities of insoluble matters, also sugar, dextrin, and aromatic constituents, besides considerable quantities of fatty bodies.

7. *Wines, beers, and spirits.*—The various kinds of wine

consist of the juice of the grape which has undergone alcoholic fermentation. Wine consists of water holding in solution alcohol, with sugar, vegetable acids and their salts, besides colouring matters, and traces of proteids. The quantity of alcohol varies from 6 to 25 per cent.; wines which contain as much as this having usually received a quantity of alcohol over and above that produced by alcoholic fermentation of the sugar of the grape. The peculiar flavour or bouquet of wines depends in great measure upon certain compound ethers which they contain.

Beer is obtained from the infusion of malt, that is, of barley which has been allowed to germinate, and in which the starch has been converted into dextrins and sugar. The infusion of malt is fermented by the addition of yeast, which converts the sugar into alcohol. The bitter flavour of beer is imparted to it by the addition of hops or other bitter substitute. The amount of alcohol in beer varies between 2 and 10 or 12 per cent. It also contains a greater or less quantity of CO_2, upon which its properties to a certain extent depend.

Spirits.—The various forms of spirit consist of water containing from 50 to 60 per cent. of alcohol. They are all obtained by first inducing alcoholic fermentation in a saccharine liquid which is thereafter subjected to distillation.

Effects following Deficient and Excessive Diet.

Before concluding this lecture, which is barely introductory to the subject of digestion, I wish to draw your attention to the effects of an insufficient and an excessive diet. Firstly, when food is entirely cut off from the body, as its losses continue, it loses weight, and the healthy and pleasurable appetite for food and drink makes place for the sufferings of hunger and thirst. The strength of the body diminishes, so that at last all exertion becomes impossible, whilst the temperature becomes much reduced.

An insufficient diet leads to results which resemble more or less closely those which attend an absolute deprivation

of food. The wasting of the body, loss of weight and lack of ability for work, are amongst the most prominent phenomena. The proclivity to particular disorders of nutrition, as for example to scurvy, no less than the tendency to become affected by zymotic diseases, has been noticed in cases where individuals and populations have been subject to the influence of deficient food. The epidemics of typhus and of relapsing fevers which have followed famine in Ireland, may serve to illustrate the fact upon which I am dwelling.

Secondly. In the case of an excessive diet various results may follow. When the amount of food taken is in excess of the wants of the economy and yet not so much as to be beyond the capacity of the body to digest it, it is observed as a rule that the weight of the body is increased, and this is due in great measure to a deposition of fat. The rapidity with which the increase in weight occurs depends however upon a large number of circumstances, as for instance on the predisposition of the body to accumulate fat, and on the amount of work done by it. In many cases, when the diet continues for long periods of time in excess of the proper demands of the system for matter and energy, there are induced functional disorders of the organs of digestion, and of the organs which are chiefly concerned in dealing with the products of digestion, as for example the liver ; or there may be induced such a disorder of nutrition as constitutes the disease gout, though in the production of this complaint alcohol is an adjuvant and almost necessary factor.

LECTURE II.

GENERAL SKETCH OF THE DIGESTIVE APPARATUS.—THE ALIMENTARY JUICES.—MASTICATION AND THE ORGANS CONCERNED IN IT.

In my first lecture I have explained to you that a supply of Food and of Oxygen gas are absolutely essential to an animal body, in order that it should manifest the phenomena which are essential to Life, for all these phenomena are associated with a dissipation from the body of Energy, which can only be obtained by a transformation, re-arrangement and elimination of certain of the matters of the body. In former times, before clear ideas had been formed as to the sources, relations and transformations of Energy, it was not absurd to speculate on the possibility of discovering agents which, whilst innocuous to life, should diminish indefinitely the waste of the body. We now know such speculations to be absurd, inasmuch as the act of living implies transformations of energy associated with transformations of matter, i.e. continual losses which have to be made up.

The needs of the animal body for matter to take the place of that which is passing away from it, are made known to it by certain sensations. The need for pure air, containing the oxygen gas which the body requires in such large quantities to oxidize or burn its organic constituents, is under normal circumstances imperceptible to us; so soon, however, as the supply of oxygen falls below the wants of the system we have a train of symptoms, ushered in by shortness of breath, exaggerated movements of respiration, and anxiety for fresh air, which not only make the organism acquainted with the special want, but likewise in many cases at once remedy the deficiency which exists.

Hunger and Thirst.

The needs of the body for solid and especially for organic food, and for water, make themselves felt by the peculiar sensations of *hunger* and *thirst.*

Hunger is a peculiarly indefinite sensation of craving or want, which is referred to the stomach, but with which is often combined, always indeed in its most pronounced stages, a general feeling of weakness or faintness. The earliest stages are unattended with suffering, and, leading the animal to wish and seek for food, are characterized as "appetite for food." Hunger is normally appeased by the introduction of solid or semi-solid nutriment into the stomach, and it is probable that the almost immediate alleviation of the sensation under these circumstances is in part due to a local influence, perhaps connected with a free secretion of gastric juice. Essentially, however, the sensation of hunger is a mere local expression of a general want, and this local expression ceases when the want is satisfied, even though only liquid and no solid food be introduced into the stomach, or even though no food be introduced into the stomach, but the needs of the economy are met by the introduction of food through other channels, as, for example, when food which admits of being readily absorbed is injected into the large intestine.

Thirst is a peculiar sensation of dryness and heat localized in the tongue and throat. Although thirst may be artificially produced by drying, as by the passage of a current of air, the mucous membrane of the above parts, it normally depends upon an impoverishment of the system in water. And when this impoverishment ceases, in whichever way this be effected, the sensation likewise ceases. The injection of water into the blood, the stomach, or large intestine, appeases thirst, though no fluid is brought in contact with the part to which the sensation is referred.

Nature of the Processes of Digestion.

The sensations, the causes of which I have attempted to analyse, lead us, or, when urgent, compel us to take food and drink into the mouth. Once in the mouth, the entrance of the alimentary canal, the food is subjected to the first of a series of processes, whose assemblage constitutes the Function of Digestion. Digestion may be defined as *the assemblage of processes, mechanical and chemical, whereby the constituents of food are rendered soluble and converted into substances which are capable of being absorbed, and afterwards assimilated.* To the precise meaning of these terms, and to the processes concerned in absorption and assimilation, I shall direct your attention in the last of this series of lectures.

A PRELIMINARY GENERAL SKETCH OF THE ORGANS OF DIGESTION IN RELATION TO THEIR FUNCTION.

I wish at the very outset to point out very clearly to you that the food which we introduce into the alimentary canal is, strictly speaking, outside the confines of the body; as much, indeed as the fly grasped in the leaves of Venus's fly-trap—the insectivorous Dionea—is outside of the plant which is to digest it.

The mechanical and chemical processes to which the food is subjected in the mouth, stomach and intestines, are processes which have their seat and conditions outside of the body which it is destined to nourish, though unquestionary the body is no passive agent, and innumerable glands have to come into action in order to supply chemical agents able to dissolve and render *assimilable* those constituents of food which are capable of being absorbed *into* the organism, and forming, as it were, part and parcel of its substance.

The processes to which the food is subjected, though manifold, are divisible into two great groups. (1) Chemical. The food must be subjected to the action of certain juices,

which dissolve insoluble alimentary matters, and modify these, besides acting upon certain of the soluble alimentary constituents in the one case, and in the other the end being to produce bodies which shall not only be *soluble*, but likewise *diffusible*.

(2) Mechanical. The food must be first broken up and crushed, more or less completely, and afterwards mechanically mixed with the digestive juices, and the mixture propelled slowly from beginning to end of the alimentary canal.

In accordance with this double set of processes—the chemical and the mechanical—which go on in the alimentary canal, it presents the form of a complex and in some regions modified tube, possessed of two openings, where it is continuous with the general surface of the body—a tube, however, which is, as it were composed of two distinct but intercalated tubes. (1) An internal tube of *mucous* membrane, and (2), investing this closely and connected with it, an external muscular tube.

I point to a rough diagram (see Fig 1) which exhibits the general arrangement of the alimentary canal, and I wish now to direct your attention to some general anatomical facts in relation to it, reserving, however, a minuter study of some of its component organs to subsequent lectures, in which a closer acquaintance with structure will be needed, in order that we may study their functions with accuracy.

You observe that the muscular membranous alimentary canal is not regularly tubular throughout. At the beginning it forms the irregular cavity of the *mouth* (M), which contains the *tongue* and the masticatory *teeth*. Thence it passes through the *fauces*, and beneath the pendulous *soft palate* and *uvula*, into the *pharynx* (Ph). Afterwards it proceeds as a regular tube, the *œsophagus*, (Œ) or *gullet*, which dilates at the cardiac orifice into the *stomach* (S), at the further, or *pyloric*, end of which the tube resumes its narrow uniform calibre, constituting at this part the small intestine which is arbitrarily divided into the *duodenum* (D), *jejunum* (J), and *ileum* (I), of which,

Fig. 1.

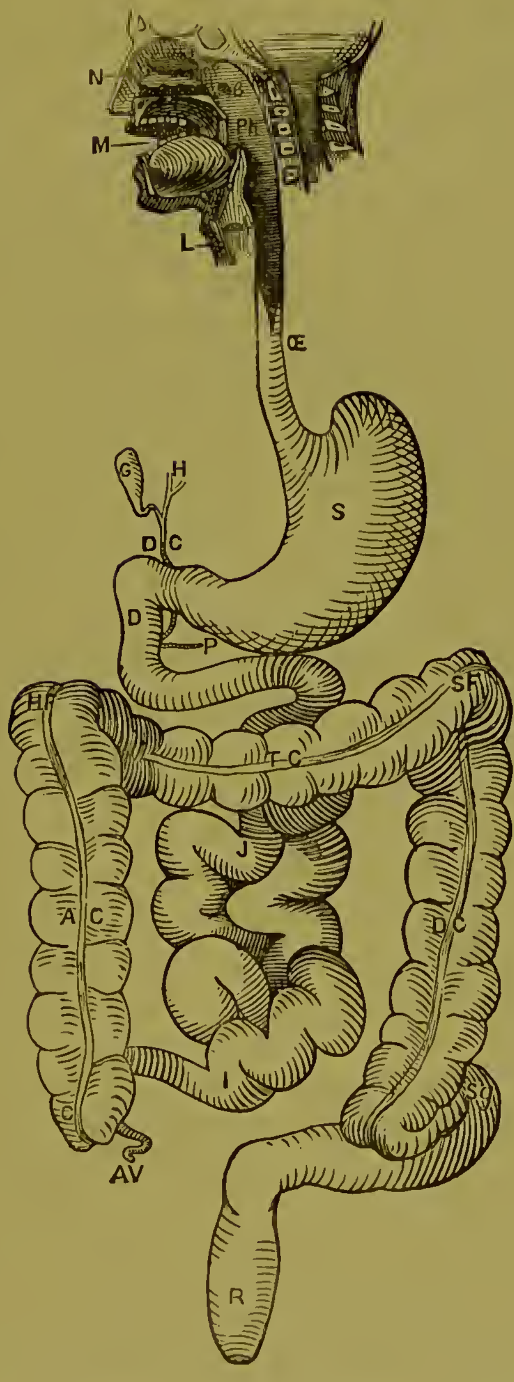


DIAGRAM OF THE SEVERAL DIVISIONS OF THE ALIMENTARY CANAL (TURNER).

M. mouth ; Ph. pharynx ; Œ. œsophagus ; S. stomach ; D. duodenum ; J. jejunum ; I. ileum ; AV. appendix vermiformis ; AC. ascending colon ; HF. hepatic flexure ; TC. transverse colon ; SF. splenic flexure ; DC. descending colon ; Sg. sigmoid fluxure ; R. rectum ; L. larynx ; E. Eustachian tube ; G. gall-bladder ; H. hepatic duct ; DC. common bile duct ; P. pancreatic duct.

in man, the duodenum occupies a length of twelve fingers, the ileum the lower three-fifths, and the jejunum the intermediate portion of the total length of 20 feet. The small intestine diminishes somewhat in calibre from duodenum to ileum, and at the lower end of the latter the small opens suddenly into the much wider larger intestine: though not at the very commencement of this, which is a cul-de-sac, the *caput cæcum coli*, but at a point a little removed from this.

The margins of the aperture by which the small gut opens into the large, project into the latter in such a manner that while they readily permit the passage of matters from small into large intestine, any backward movement of the contents of the large intestine would have the effect of compressing the lips of the opening and closing it; this arrangement constitutes the so-called *ilio-cæcal valve*. Connected with the *caput cæcum coli* is a small diverticulum like a narrow glove finger, called the *vermiform* appendage (A V). The first and greater part of the large intestine is known as the *colon*, the last as the *rectum* (R). The colon is subdivided into ascending colon (A C), transverse colon (T C), and descending colon (D C), the bend made by the transverse in passing into the descending colon receiving the name of the *sigmoid flexure*. (S) The lower orifice of the rectum is the anus. The total length of the large intestine is from five to six feet.

Both muscular and membranous (mucous) tubes are continuous from mouth to anus, and at these, the superior and inferior orifices, the *mucous membrane*, which constitutes what we have hitherto termed the membranous tube, is continuous with the skin which covers the general surface of the body. This mucous membrane is covered throughout at its free surface by a layer or layers of cells, the so-called *epithelium*, and gives lodgment to glands, whose characters differ in different parts of the tube in accordance with the function of the part. Below the epithelium is a connective tissue analogous to the true skin, which in parts has the character of ordinary fibro-areolar tissue, but in all parts from the stomach downwards has the character of so-called *adenoid connective tissue*, as it is found in the follicles of lymphatic glands. Its meshes support a rich supply of fine blood-vessels, lymphatic vessels, and doubtless also of delicate nervous filaments. Besides these elements there are found numerous small

bundles, or in parts even sheets, of *involuntary muscular fibres*, which probably give to the mucous membrane the power of limited self-contraction, of such a nature as to further the flux and reflux of fluids in the myriad lymphatic vessels of the part, and perhaps to influence in no small degree the outpouring of the secretion of certain of the glands. To the fairly continuous tract or sheet of involuntary muscle which lies at the base or deepest part of the mucous membrane the term of (tunica) *muscularis mucosæ* is applied.

In addition to the glands which lie embedded in and open upon the surface of the mucous membrane of the alimentary canal, others of larger size and not in immediate relation with its walls communicate with the interior of the tube by ducts which open into it, and which pour into it their secretion; such glands are the salivary glands, the pancreas, and the liver.

The muscular tube in the greater part of its extent consists of two layers of involuntary, non-striated, pale, muscular fibres—an inner whose fibres encircle the tube, and an outer whose fibres run parallel to the long axis of the tube. But this is not the arrangement of every part. In the stomach there is an apparent rather than a real exception, where some layers of fibres of the circular coat course over the dilated walls of the alimentary tube in an oblique direction, giving rise to an oblique layer. In the œsophagus or gullet, besides the typical, circular, and longitudinal layers, there is at the upper part a second longitudinal layer which takes up a position internal to—that is, nearer—the mucous membrane than the circular layers. In the upper part of the gullet also the muscular fibres are not unstriped, but, although certainly involuntary, are striated like voluntary muscles.

In the mouth the muscular tube is most irregular and most defective, for the mucosa is in parts directly applied to the bony boundaries, as over the hard palate and gums; in another part it invests the muscular prominence of the tongue; whilst in other regions it lies upon the constrictors of the pharynx and the inner aspect of certain other muscles, as those of the cheeks, lips, and floor of the mouth. The membranous tube is united to the muscular tube by a loose layer of connective tissue containing many blood-vessels and lymphatic vessels and nerves for the supply of the mucosa; it is often called the *submucosa*.

The mucous membrane is the seat of various secreting glands, which lie embedded in its substance and open upon its surface,—simple or branched tubular recesses running through the depth of the layer, lined by epithelium, continuous with, though not always resembling, that of the surface, and opening at the surface by minute pores. In the mouth, pharynx, and œsophagus those form the *acinous* or *racemose* glands, which, according to certain subordinate features which they present, and also according to certain of the characters of the fluids which they secrete, are separated into *mucous* and *serous* glands.

In the stomach they are represented by the simple or branched tubular gastric glands. In the duodenum we find them as simple tubular deep sockets, the crypts or glands of Lieberkühn, and also as the compound, acinous glands of Brunner, which dip below the level of the mucosa and lie in the submucosa. In the jejunum, ileum, and large intestine they form again the crypts or follicles of Lieberkühn.

The membranous tube is not everywhere exactly concentric and conterminous with the muscular tube. In the mouth and pharynx this is so almost entirely, but at the gullet the muscular tube so tightly encloses the membranous that the latter is forced into longitudinal plications to find room for itself. In the stomach the membranous layer is raised into ridges or *rugæ*, which intersect and give the surface a honeycomb-like aspect. In the upper part of the small intestine the membranous tube is raised into deep annular or, more correctly, crescentic folds, running across the direction of the gut like incomplete diaphragms, or a series of membranous ledges; these are the *valvulæ conniventes*. In the colon the two tubes are so disposed as to form a regular series of saccules or pouches, greatly enlarging the capacity of the gut. All these foldings greatly enlarge the superficies of the membranous tube. A further enlargement is effected in the small intestine in an exceedingly interesting fashion; the surface of the mucosa is thickly studded with innumerable, fine, short projections resembling the pile of velvet. These are invested by surface epithelium, and amongst them, at their feet, open the before-mentioned *crypts of Lieberkühn*. They are the so-called *villi*. Each contains a lymphatic vessel, blood-vessels, and involuntary muscular fibres, all supported by adenoid connective tissue like that of the mucosa below; the lymphatic is in the axis of the villus, the muscles form the next layer, and the blood-vessels lie immediately beneath the epithelium. When the muscular layer of the villus contracts it must of necessity compress the lymph vessel, whilst causing no impediment to the flow of blood.

We have described the mucous membrane of the stomach and intestines as containing a framework of adenoid reticular tissue like the tissue of lymphatic follicles. It is, indeed, identical with this,—a network of branched cells with oval nuclei, and the meshes of which are crowded with lymph corpuscles with round nuclei. At certain points in the intestines the adenoid tissue of the mucosa presents local nodular enlargements; the mucosa at these points becomes so much thicker that it swells up at the free surface beneath the epithelium into rounded eminences about as large as millet-seeds or the heads of small pins; and at the under surface of the mucosa it dips into the submucous tissue in a similar manner. At the base of this nodule of adenoid tissue in the submucosa there is usually a network of wide, thin-walled, lymphatic vessels. Many of these rounded masses are scattered irregularly over small and large intestine as the *solitary follicles* or *glands*, but at the lower end of the ileum they form little colonies, often covering an area an inch or more in length, and they are situated at

that part of the intestine which is remote from the attachment of the mesentery. They then constitute the so-called *Peyer's patches.*

Nodular adenoid masses are, however, not limited to the adenoid mucosa of the intestines. They are occasionally, though rarely, found n the stomach; they exist beneath the mucous membrane of the tongue, and a colony of them forms the mass of the *tonsil* on each side,—that almond-shaped body situated between the posterior and anterior pillars of the fauces.

The intrinsic nerves of the alimentary tube consist of two systems of nervous networks with ganglion cells lying at the nodes ; one is found in the submucous layer (' Plexus of Meissner '), the other lies between the longitudinal and circular muscles (' Plexus of Auerbach.')

The whole of the intestines, and the stomach as well, are sustained in the abdominal cavity by sheets of delicate membrane, formed by folds of peritoneum, and called, in the case of the intestinal portion of the tube, the *mesentery.* Between the layers of the mesentery run the vessels and nerves for the supply of the bowel. In addition to blood-vessels there are numerous thin-walled lymphatic vessels called *lacteals*, which are fed by the rich network of lymphatic vessels of the mucosa and submucosa, and which run in the mesentery to the back of the abdominal cavity. Here they are collected into a large lymphatic reservoir, the *receptaculum chyli*, from which a duct, the *thoracic duct*, proceeds along the side of the vertebral column to open into the venous system at the junction of the subclavan and jugular veins on the left side of the neck. The lacteal and lymphatic vessels, whose course has been briefly sketched, are interrupted at many points by the presence of lymphatic glands. These may be simply regarded as labyrinthine systems of vessels into which the simple *afferent* lymphatic or lacteal vessels open, and each of which is surrounded and penetrated by adenoid connective tissue, like that of the intestinal mucosa. The lacteal vessels after food are filled with a milky fluid, the *chyle.* They were discovered by Aselli in the year 1662.

It must not be thought that the glands of the mucous membrane of the alimentary canal are alone engaged in the preparation of the solvent digestive fluids. Other organs lying away from the alimentary canal pour their secretions into it by ducts at various points. In the neighbourhood of the mouth there are three pairs of *salivary glands ;* the *parotid* glands, lying outside the cheek over the lower jaw, just in front of the meatus of the ear. The ducts of the pair course along the cheeks and pierce them opposite the second upper molar tooth on each side. These are the two ducts of Stenson. A second pair, the *sub-maxillary*, lies beneath the ramus of the lower jaw and beneath the floor of the mouth ; their ducts run forward to open beneath the tongue : these are the ducts of *Wharton.* The third pair, the *sublin-gual*, lies on the floor of the mouth, beneath the mucous membrane anterior to the openings of the ducts of Wharton. The ducts of these glands are numerous, and open by many apertures on the floor of the

mouth, some opening into the ducts of Wharton. These constitute the ducts of Rivini.

About three or four inches below the pylorus the ducts of two large glands open into the small intestine by a common orifice; these are the pancreatic duct, from the pancreas on the left, and the common bile duct from the liver on the right.

The Alimentary Juices the products of Secreting Glands.

Having made a general survey of the anatomical arrangements of the alimentary canal, before commencing a detailed study of the digestive processes, I wish to draw your attention to certain important general facts connected with the alimentary juices.

I have already told you that the processes of digestion depend essentially upon these juices, which require for their proper action certain physical conditions, and are aided by certain mechanical operations.

These juices, which we shall study in detail under the several titles of saliva, gastric juice, pancreatic juice, bile, and intestinal juice, are all the products of organs termed *secreting glands*, because they are engaged in separating or *secreting*, at the expense of matters derived from the blood, the liquids which form their characteristic *secretion*. The secreting glands of the alimentary canal may be considered to have been formed by an involution of the mucous membrane which lines it, which may either be simple, test-tube like, as in the so-called glands of Lieberkühn, or exceedingly complex as in the salivary glands or the pancreas. These glands have in some cases distinct ducts or passages which establish a communication between the inner secreting recesses and the alimentary canal, but in all cases they contain, as essential elements, cells of *secreting epithelium*—their so-called *secreting cells*—whose function it is to form the matter of the secretion. All glands are abundantly supplied with blood-vessels, and a like meshwork of capillaries is in close proximity to the microscopic secreting cells; there are, in addition, invariably nerve fibres supplying the gland, though it cannot be said

that the exact connection of fibres with gland cells has yet been traced.

The secreting cells do not draw their nutriment *directly* from the blood, but from the liquid—the lymph—which has transuded from the minutest blood-vessels, *the capillaries*, and which bathes the anatomical elements of all tissues and organs ; from this transuded liquid the gland cells obtain both oxygen and liquid and solid matters, and to it they contribute certain products of waste which subsequently make their way into the blood, and are thence got rid of through the intermediation of such excretory organs as the lungs, the kidneys and the skin.

The digestive juices are all of them liquids which contain very much water ; in this respect the saliva may be taken as an example, for it rarely contains more than four or five parts per thousand of solids.

The first idea which was formed of the process of secretion was that it resembled closely, if it was not actually identical with, a process of straining or filtration, and the properties possessed by the liquid products of various secreting glands were supposed to depend upon the different characters of their filtering arrangements.

It was afterwards supposed that secretion was more allied to the processes of *osmosis* and *diffusion*, by which movements of liquids and a separation of the solid constituents which they contain may be effected through the agency of thin membranous septa.

These purely physical explanations have, however, been disproved, and I have to tell you that, although influenced by certain of the circumstances which affect filtration, and though doubtless also thus connected with osmotic and diffusion phenomena, *secretion* essentially depends upon the activity of the living anatomical units of the glands, the gland cells. The matter of these cells—their *protoplasm*—possesses as an inherent property the power of abstracting certain matters from the lymph and leaving others, and more than that, of actually manufacturing at the expense of certain of the matters of the lymph, new bodies,

which give special characters to the secretions of particular glands.

During life the activity of these gland cells appears to be influenced both by changes in the blood supply of the whole gland, which are brought about through the agency of nerves distributed to their blood vessels, and by a direct action exerted upon the gland cells by certain nerve fibres which are able to bring about changes in the processes of the cell even independently of changes in the blood supply, even indeed (for a limited period), in the absence of any blood supply.

These alimentary juices which are most active in digestion, particularly the gastric juice, and the pancreatic juice, owe their activity, as we shall see, to the presence in them of certain bodies which have been classed amongst *ferments*, though they differ in many important particulars from the most characteristic ferments.

By the term ferment we usually designate bodies which, even in minute proportions, possess the power of bringing about in particular substances with which they are brought into relation, and under favourable circumstances, chemical changes of great magnitude. The most characteristic ferments are the so-called *organised* or *formed ferments*, of which yeast affords us an admirable example. The action is here necessarily linked with the life of the yeast cell, and it is only so long as the cell is intact and living that it can bring about the characteristic alcoholic fermentation of sugar.

Anything which destroys the organism with which the ferment action of a true ferment is linked, renders it inert; this ferment action cannot therefore be abstracted from the organic form by solvents.

But the term *ferment* has been applied to other bodies which doubtless are definite chemical proximate principles (though as yet we have not succeeded in separating one in a state of such purity as to warrant our stating its precise chemical relations), which are the products of the activity of certain living cells, but which having been once formed

are no longer dependent upon the life of the cell, and may indeed be extracted from it by appropriate solvents, of which glycerine is the most generally available and the best example.

The ferments of the second class are often termed unformed or unorganised ferments. They resemble the organised ferments in their origin in living cells, and in the power which they possess of bringing about chemical changes on a very large scale. But they differ in many other respects, especially in this, that they do not develop or increase whilst their action is being excited. It is ferments of this class which are present in the alimentary canal. It has been suggested by Kühne that the term *Enzymes* should be applied to the unformed ferments of the animal body.

The living gland cells of certain of the glands of the alimentary canal appear in the first instance to manufacture bodies which are, as it were, antecedents of the ferments or enzymes, to which the generic term of *Zymogens* has been given. Then zymogens, appear under various conditions to liberate the active and fully formed enzymes.

MASTICATION.

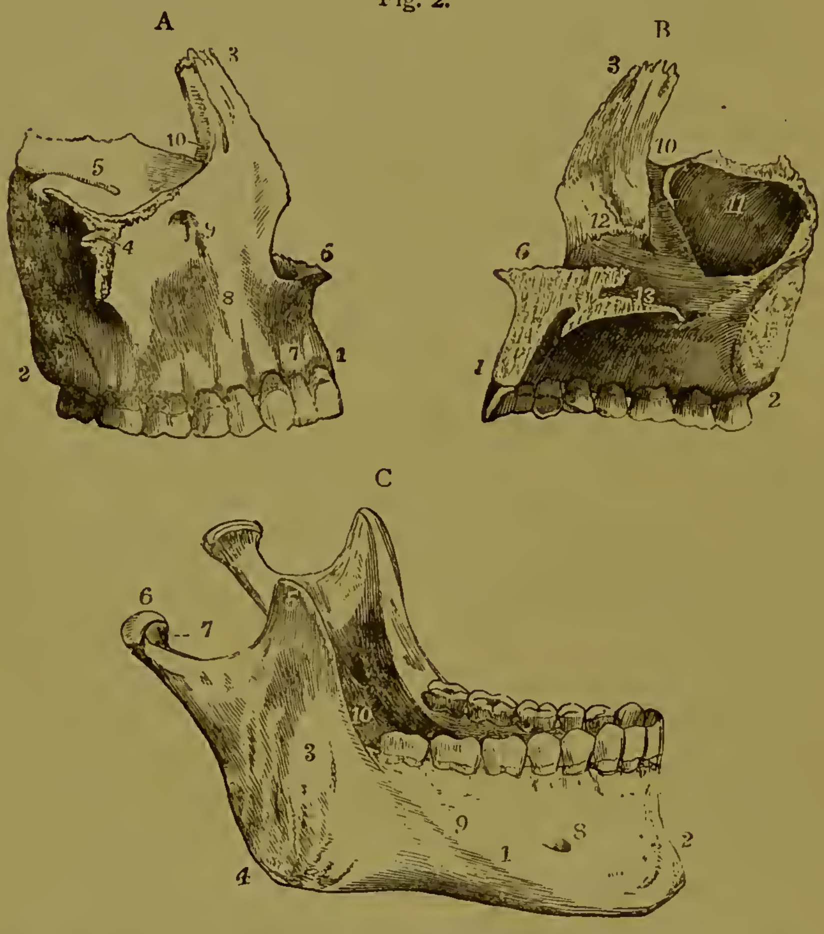
We shall commence the study of the digestive process by an examination of the process of mastication, by which the food is reduced in the mouth to so minute a state of division as enables the nutritive juices which come in contact with it to act with advantage. We cannot obviously understand the process of mastication, unless we know something of the structure and mode of arrangement of the teeth, which are the organs specially concerned in it, of their relation to the maxillary bones, or jaws, in which they are implanted, and of the principal muscles which act upon the jaws.

Structure and arrangement of the Teeth.

Nearly all mammals have teeth forming the essential part of the masticatory apparatus, and in a majority of

mammals, as in man, the teeth are not all of one shape, but present distinctive peculiarities, which are related to the functions which they have to perform. In most, though not in all mammals, we observe, moreover, that we

Fig. 2.



THE SUPERIOR AND INFERIOR MAXILLARY BONES (QUAIN'S ANATOMY).

A. Superior Maxillary Bone of the right side from the outside.
B. The same bone seen from the inside.
C. The Inferior Maxillary Bone seen from the right side and above.

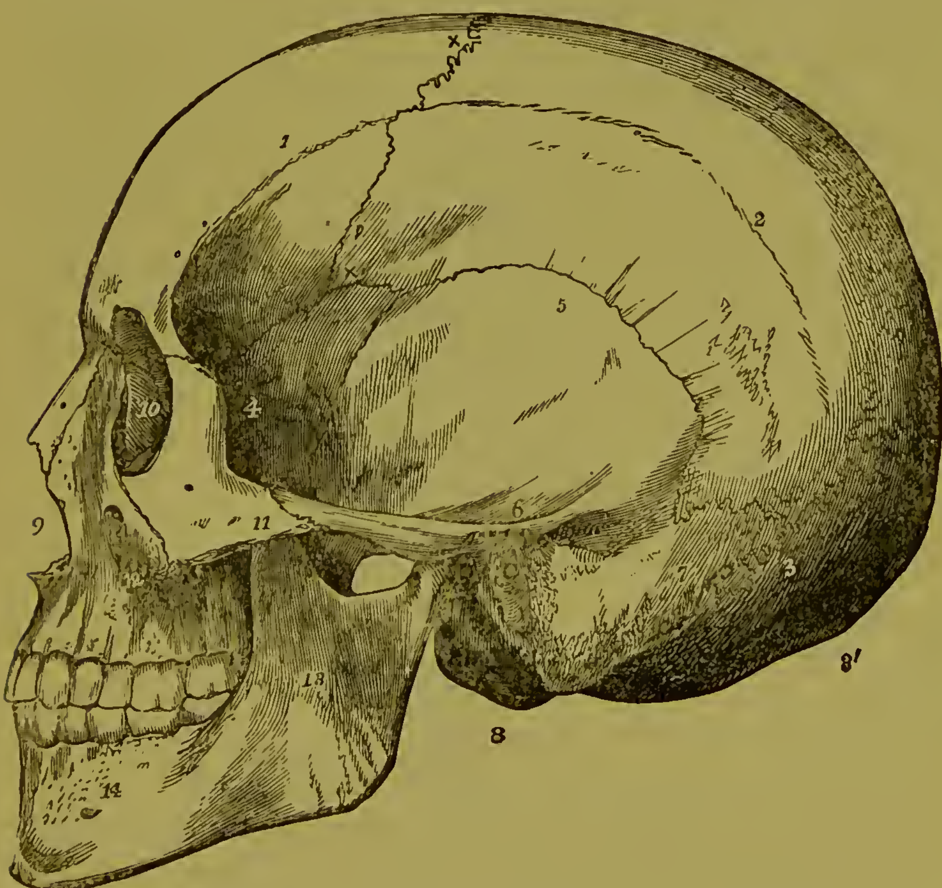
have more than one set of teeth, a first or deciduous set which is shed, and which is succeeded by a permanent set.

The teeth are imbedded in sockets, so-called *alveolar cavities,* which are contained in the *superior* and *inferior maxillary bones.*

We find both the deciduous and permanent teeth arranged

in the form of two nearly symmetrical rows, an upper row and a lower row. The teeth of the upper row are connected with the alveolar arches of the two superior maxillary bones, or upper jaw bones (see Fig. 2, A. and B.) which, although in close apposition, remain distinct bones throughout life. The teeth of the lower set are imbedded in sockets in the inferior maxillary or lower jaw bone (see

Fig. 3.



LATERAL VIEW OF THE SKULL (QUAIN'S ANATOMY).

Fig. 2, C.) This, which is the only moveable bone of the skull, in the early stages of existence is double, but the two portions subsequently unite in the middle line at the so-called *symphisis* (C. 2), to form a bone having somewhat the form of the horse-shoe. The diagram to which I now point (Fig. 3), must be looked at side by side of the one

which we have just examined. You here see the superior maxillary bones in their complicated relations to the other bones of the face: the relation of the inferior maxillary bone to the cranium: and of the upper to the lower set of teeth. You notice (Compare also Fig. 2, C.), that from the back part of the inferior maxillary bone there ascends almost vertically a part of the bone, technically termed its *ascending ramus*, which terminates above in two processes, the anterior of which, the *coronoid process*, serves for the attachment of the powerful *temporal* muscle, whilst the posterior process, the *condyle* of the inferior maxilla, presents an articular surface covered with cartilage, which fits into a corresponding articular cavity termed the glenoid fossa, on the lower surface of the temporal bones; there being, however, an intermediate plate of gristle (inter-articular fibro-cartilage) between the one articular surface and the other.

In the human adult in the perfect condition, 16 teeth exist in each jaw, viz.: 4 *incisors*, 2 *canines*, 4 *bicuspids*, and 6 *molars*. These, though differing somewhat in form, yet present many characters in common. Anatomists have divided every tooth into three parts, viz.: the crown, the root or fang, and the cervix or neck. The crown is the part of the tooth which projects above the gum, and which is covered by the hardest of all the tissues of the tooth, the so-called *enamel*; the fang is imbedded in the alveolar cavity, whilst the cervix is the somewhat constricted part of the tooth which is embraced by the gums.

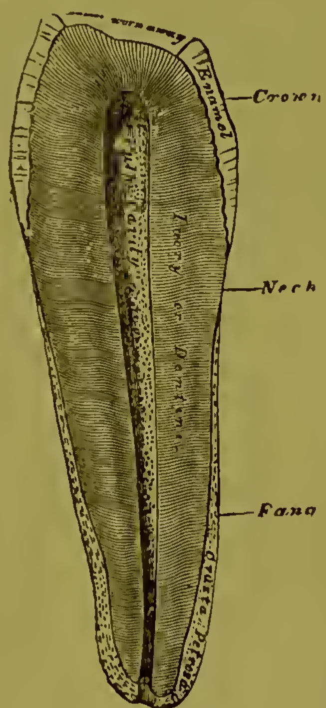
Look at the diagram of the section of tooth to which I now point (Fig. 4), and you will observe not only the parts of the tooth to which I have referred, but also certain other appearances to which I wish to call your attention.

The crown is seen to be covered with a thin layer of the very hard *enamel*, which is found on microscopic examination to be made up of columns of hardened fibres, which remind us somewhat of columns of basalt, and which contains about 96 parts in 100 of mineral matters.

The greater part of the tooth is made up of the structure termed *dentine* or ivory, having essentially the same

chemical composition as bone, but which is seen to be perforated by innumerable tubules, the *dentinal* tubules. The outline of the fang is seen to be covered by a thin layer of a tissue, which presents certain of the anatomical elements of bone and which is termed the *crusta petrosa.* The centre of the tooth you will observe is hollow; here we have the so-called *pulp cavity.* In the living condition this cavity lodges a very vascular structure, "*the pulp*," composed of connective tissue, which supports

Fig. 4.



VERTICAL SECTION OF A BICUSPID TOOTH, MAGNIFIED (GRAY'S ANATOMY).

blood vessels and nerves. Certain cells of the pulp, so-called '*Odontoblasts*' have processes connected with them and it is these processes which probably enter the dentinal tubules. You will observe that a canal perforates the fang or fangs; it is through this that blood vessels and nerves pass to and from the pulp, and establish a nervous and muscular connection between it and the maxillary bones in the first instance.

Before examining, in as detailed a manner as the short space of time at our disposal permits, the characters of the permanent teeth of man, let me mention two interesting facts: firstly, that the teeth are structures which are formed by a modification of the tissues which enter into the composition of the mucous membrane of the mouth; and, secondly, that the jaws of the toothless infant at birth contain already formed, in great measure, the teeth of the milk set, and, stored away in so-called *cavities of reserve*, the rudiments of nearly all the permanent teeth.

The number and character of the teeth is indicated by anatomists by means of so-called *dental formulæ*, which I may remark, have nothing in common with mathematical formulæ. I shall illustrate the use of these formulæ by writing down before you the formula of temporary dentition and then that of permanent dentition in man.

In these misnamed formulæ we have first of all a vertical line in the centre to indicate the separation between right and left maxillæ and a horizontal line to indicate the separation between teeth of the upper and of the lower jaws. The letters which are above the numbers indicate the characters of the teeth enumerated; thus. *i.* stands for incisor; *c.* for canine; *p.m.* for praemolar; *m* for molar. The formula allows us to see at a glance the position of the teeth in the jaws.

FORMULA OF TEMPORARY DENTITION.

m.	c.	in.	in.	c.	m.	
2	1	2	2	1	2	= 20
2	1	2	2	1	2	

FORMULA OF PERMANENT DENTITION.

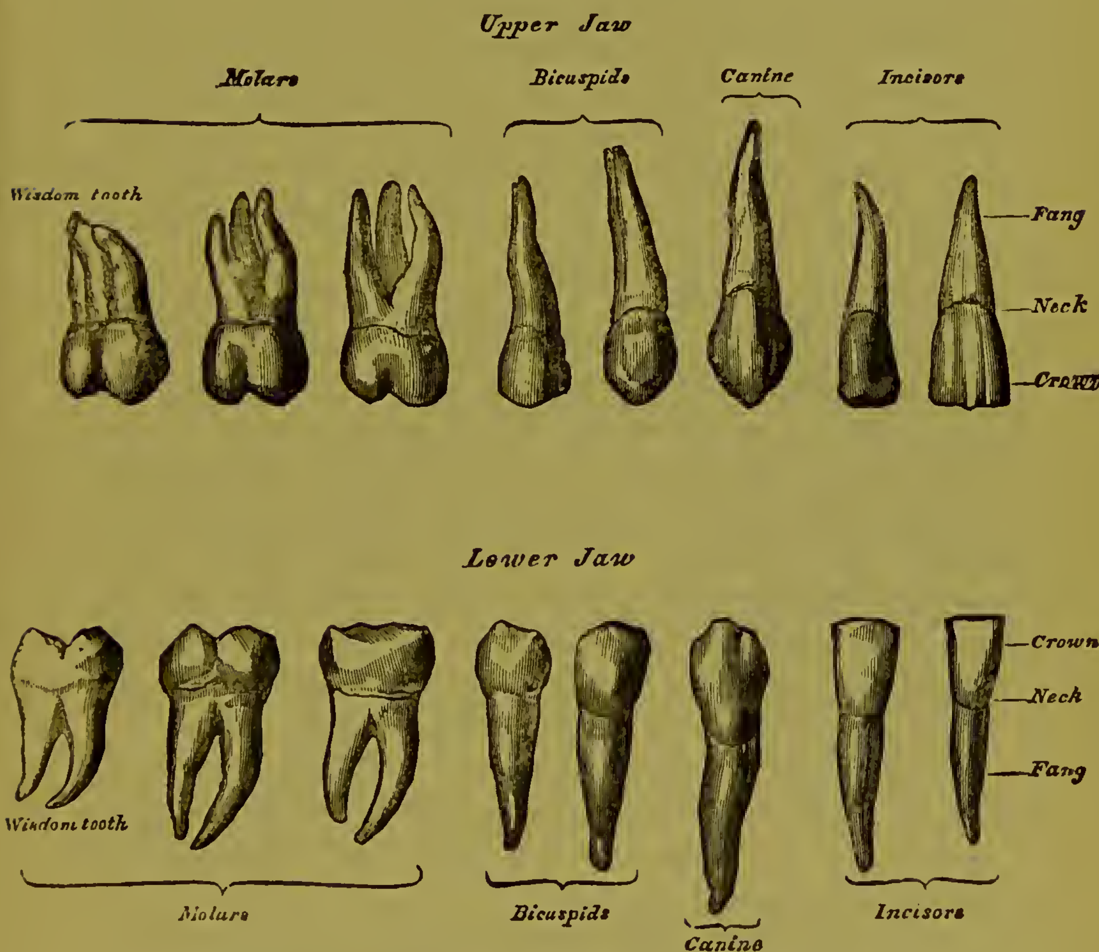
m.	pm.	c.	in.	in.	c.	pm.	m.	
3	2	1	2	2	1	2	3	= 32
3	2	1	2	2	1	2	3	

Let us now examine very briefly the characters of the different teeth in the adult jaw (Fig. 5).

1st. The incisors. These are eight in number, two on

each side of the middle line both in the upper and lower jaws. Observe the chisel-like cutting edges of these single-fanged teeth, their somewhat convex anterior surface, the little eminences with intervening notches presented by the typical tooth before its cutting surface has been worn down

Fig. 5.



THE PERMANENT TEETH, EXTERNAL VIEW (GRAY'S ANATOMY).

by hard usage, and the fact that the central incisors of the upper jaw are larger than the lateral incisors, whilst the opposite holds true of the lower jaw.

2nd. The canines, four in number, one on each side in each jaw. Note their very long fang, the great convexity of the anterior surface, and its angular point. These are

the teeth which are so largely developed in the dogs and the cats, and which in these creatures are used for tearing their food.

It will be observed by comparing the two dental formulæ before us, that the number of incisors and canines is the same in the child and in the adult.

3rd. The praemolars, eight in number altogether, are not represented in the dental formula of the child.

Observe the broader surface of the crown, as contrasted with that of the teeth we have yet examined; from its presenting two tubercles or *cusps*, these teeth have often been called *bicuspids*. Note that their fang is grooved, indicating that it is composed of two imperfectly coalesced fangs.

4th. The molars, twelve in number altogether, are square topped, offering a broad surface, which is rendered uneven by the four or five cusps or prominences which each presents. Such a surface as fits these teeth to be, as their name implies, *the grinders*. Observe the three strong and curved fangs of the upper molars, the two fangs of the lower molars, each one of which with a groove which indicates generally its bified character. To the most posterior of the molars, as you all know, the name of *wisdom teeth* is given, from the fact of their eruption usually occurring when adolescence has passed, and adult life been entered upon.

Looking now at the skull which I hold in my hand (see Fig. 3), I wish to direct your attention to the fact that the teeth of the upper jaw form a wider arch than, and slightly overhang, those of the lower.

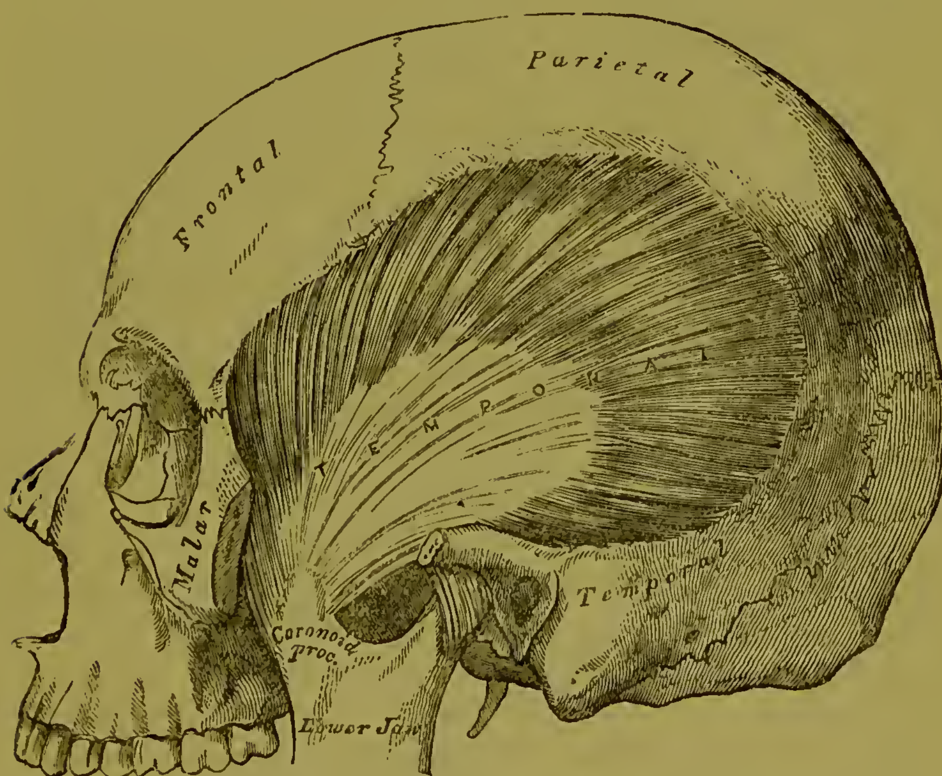
This depends upon the circumstance that the anterior teeth in the upper jaw have a direction obliquely forwards, and the posterior teeth slant outwards, whereas the lower incisors are vertically placed, and the teeth posterior to them are directed inwards. When the jaws are placed in apposition, the teeth of the upper correspond to the intervals between those of the lower jaw; this is brought about by the upper incisors being larger than the lower. Nevertheless the two dental arches terminate nearly in the same vertical

plane posteriorly, because of the larger size of the wisdom teeth of the lower as compared with those of the upper jaw.

Movements of the Human Jaw.

The human inferior maxilla, or lower jaw, admits of three different movements: 1stly, A movement of opening and shutting: 2ndly, A movement of advancing and retiring, in

Fig. 6.



THE TEMPORAL MUSCLE, THE ZYGOMA AND MASSETER HAVING BEEN REMOVED (GRAY'S ANATOMY).

which the whole inferior maxilla takes part; and 3rdly, a lateral movement, caused by a modification of the second.

1. *Movement of Opening and Shutting.* The inferior maxilla possesses a condyle (Fig. 2, C), which fits obliquely into the glenoid cavity of the *temporal* bone. This cavity is bounded outwardly by a transverse eminence—the 'emi-

nentia articularis' of human anatomists. The articular eminence enters into the formation of the joint, both it and the glenoid cavity being covered with cartilage.

When the mouth is slightly opened the condyle remains in the glenoid cavity, but if opened widely the condyle advances upon the articular eminence and slips back again when the mouth is closed. The use of the advancing movement of the jaw is to bring the lower row of teeth for a moment in apposition with the upper, and to cut the food as if with a pair of scissors by the retiring movement of the inferior maxilla.

The muscles which are chiefly concerned in raising the upper jaw and closing the mouth are the *masseter*, *temporal*, and *internal pterygoid:* all powerful muscles, stretching from the fixed upper jaw and skull to the moveable lower jaw. Of these the *temporal* muscle arises, as you observe, from the side of the head and behind the temples, and is inserted into the so-called *coronoid process* of the lower jaw bone (Fig. 6). The contractions of this powerful muscle are well seen during the act of mastication in old men whose temples are growing bald. The next muscle, the *masseter*, arises from that strong ridge of bone—the so-called *zygomatic arch*, which may be traced by the finger from the front of the ear to the prominence of the cheek, and is attached to the outer side of the lower jaw ; its contraction may be very plainly felt by placing the finger-tips firmly against the part of the cheek corresponding to the ramus of the jaw, while the teeth are strongly clenched. You may see it in the diagram to which I now point, and to which I shall specially direct your attention in connection with the salivary glands (Fig. 7).

The third muscle of this set is the *internal pterygoid*, which arises from the under portion of the cranium and certain bones of the face, and is attached to the inner surface of ramus of the lower jaw (Fig. 8).

The opening of the mouth is an act which depends partly upon the cessation of contraction of the muscles which close the jaw, partly upon the action of gravity, and

partly upon the contraction of certain muscles, and especially of the so-called *digastric* muscle.

The antero-posterior movements of the lower jaw are effected by means of the external pterygoid muscles (Fig. 8) on each side. These arise from the back of the upper jaw bone, and from certain other bones of the

Fig. 7.

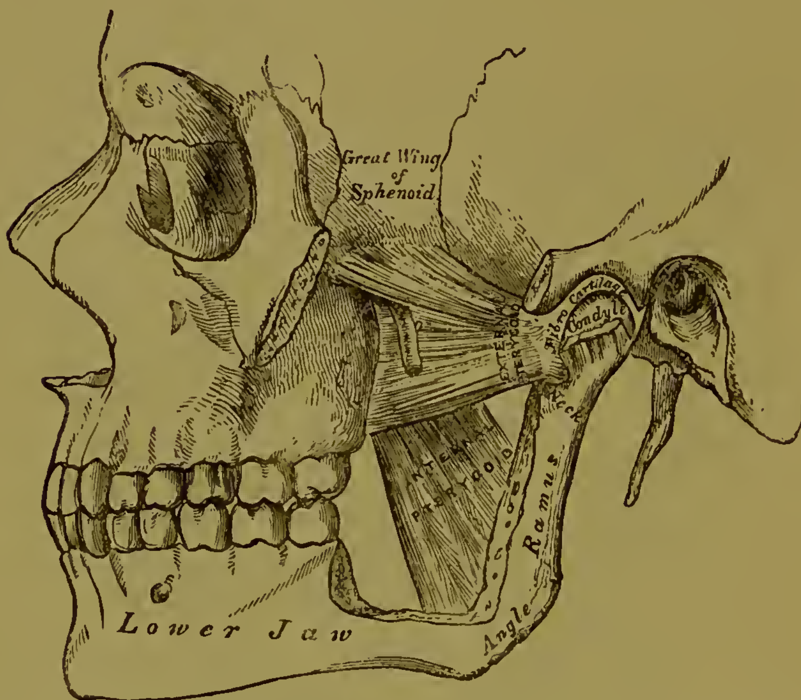
THE SALIVARY GLANDS (GRAY'S ANATOMY).

skull, and stretch in a direction backwards and outwards, to be inserted into the articular process of the lower jaw bone below the articular head. The joint action of the muscles of both sides will project the lower jaw, while the action of one only will tend to sweep the lower jaw round the opposite articulation as a pivot. It is in this way, then, that the lateral movement is effected.

By a combination of the movements which have been described, the biting, pounding and grinding movements of the jaws are effected, which in combination constitute mastication.

It must be pointed out, however, that this mechanical process is greatly aided, firstly, by the pouring out of the

Fig. 8.



THE PTERYGOID MUSCLES, THE ZYGOMATIC ARCH AND A PORTION OF THE RAMUS OF THE JAW HAVING BEEN REMOVED (GRAY'S ANATOMY).

liquid secretion, the saliva, which moistens the food, and prevents its adhering to the sides of the mouth, and afterwards binds together the fragments into a coherent mass or *bolus;* secondly, by the muscles of the cheeks, lips, and tongue, which by their contraction, prevent the matter undergoing mastication from accumulating between the cheeks and lips on the one hand, and the dental arches on the other, and also knead the food into a bolus, and force it between the surfaces of the teeth.

It is difficult to exaggerate the importance of the act of

mastication. When improperly performed, either because of a mere vicious habit of bolting the food, or because of loss of teeth, dyspepsia or indigestion is a frequent, and, sooner or later, the almost necessary consequence.

The digestive juices, whose action we shall study in subsequent lectures, cannot adequately exert their action unless the food have been previously reduced to a moderately fine state of division. The digestion of large masses of food, say by the gastric juice, must, of necessity, be much slower than if they had been broken up into many smaller fragments.

LECTURE III.

THE SALIVARY GLANDS.—SALIVA AND ITS ACTION UPON THE CONSTITUENTS OF FOOD.

THE interior of the mouth is continually moistened by a somewhat viscous, tasteless watery liquid, the *Saliva*, a product of the activity of several so called *Salivary Glands*; the presence of this liquid facilitates the movements of the lips, tongue and cheeks in articulation.

Though essential to proper articulation, the saliva is, however, to be looked upon as one of the digestive juices, and is poured out in much increased quantities when food is introduced into the mouth.

It acts as a solvent of many savoury substances, and as the vehicle which brings them into contact with the end organs of the nerves of taste; by moistening the food it renders more easy the preliminary act of mastication; it prevents the particles of food from adhering to the interior of the mouth, and thus co-operates with the muscular movements of the lips, tongue, and cheeks, in forming the crushed food into a *bolus* which may readily be propelled through the pharynx and oesophagus; lastly, in man and several other animals it exerts, in virtue of the presence of an unformed ferment or *Enzyme*, which is sometimes called "*Ptyalin*," but now more frequently the '*Diastatic*' or '*Amylolytic Ferment*' of the saliva, or '*Salivary Diastase*,' a solvent action upon the starchy constituents of food, and thus initiates the chemical operations to which the food is subjected in its passage through the alimentary canal. The saliva exerts,

therefore, two sets of functions, the mechanical and the chemical, of which the first are unquestionably the most important, as is shown by the fact that in most animals the saliva is free from disastatic ferment, and therefore from any chemical activity whatever.

Situation and Structure of the Salivary Glands.

The glands chiefly engaged in the secretion of the saliva are firstly the Parotid Glands, secondly the Submaxillary Glands, thirdly the Sublingual Glands (see Fig. 7).

The Parotid Glands, situated in front of the ear, and in great part hidden behind the ascending ramus of the lower jaw, are in man the largest of the salivary glands, varying in weight between half an ounce and a whole ounce. Each gland has a duct, known as Steno's duct, after the anatomist Steno, who discovered it in 1660. This duct, whose length is about 2½ inches, runs over the masseter muscle, and opens on the surface of the mucous membrane of the mouth, at a point opposite the interval between the first and second molar teeth of the upper jaw.

The *Submaxillary Glands*, one on each side, lie under shelter of the lower jaw, in a space termed by anatomists the submaxillary triangle. They are in man smaller than the parotids, and usually only weigh half as much. Each gland has a duct, termed, after its discoverer, *Wharton's duct*, which opens on the summit of a small papilla on either side of the so-called *fraenum linguae.*

The *Sublingual Glands* are the smallest of the three pairs of salivary glands, each being about one half the size of a submaxillary gland. They are situated beneath the mucous membrane of the floor of the mouth, on either side of the fraenum. The sublingual glands discharge their secretion by several small ducts, which open on the floor of the mouth, and to which the name of the *ducts of Rivini* is given.

In addition to the three pairs of salivary glands which I have just enumerated to you, there are numerous glands

stationed in the mucous membrane of the mouth, and especially in that covering the base of the tongue, which contribute to the formation of the saliva,

In structure, all the salivary glands present striking points of similarity, and indeed until recent times they were supposed to be identical.

They all belong to the class of acinous, or compound racemose glands, i. e., of glands which may be divided into so called lobes, each of which depends from, and is connected with a duct, which uniting with other lobar ducts forms the principal duct of the gland, the whole arrangement reminding one of a bunch of grapes.

The main duct, as well as the largei subdivisions, of such a gland as the parotid is lined with cylindrical epithelium ; as the duct subdivides, the character of the epithelium undergoes certain variations with which I need not trouble you. Ultimately, however, the gland duct leads us to the ultimate secreting *acini*, which are usually more or less tubular in form. These secreting recesses are lined by the secreting epithelium cells, which lie upon a so-called basement membrane, which is a transparent thin membrane constituting the most superficial part of the sub-epithelial tissue. Outside of this basement membrane are lymph spaces and meshworks of capillaries.

Whilst all the salivary glands present points of great resemblance, both in structure and functions, they are now subdivided into two groups.

According to the researches of Heidenhain, the glands belonging to these groups may be denominated Serous, or albuminous, and Mucous glands, according to the structure of the cells of their acini, their chemical characters, and the nature of the secretion which they elaborate.

To the group of Serous Glands belong the parotid of man and the majority of animals, the submaxillary gland of the rabbit, and some of the glands of the tongue ; to that of Mucous Glands belong the submaxillary and sublingual glands in most animals, some of the glands of the tongue,

and the œsophageal glands. Glands belonging to the former of these classes secrete a fluid containing some though it may be only a small quantity, of a proteid, coagulable by heat, and resembling, if not identical with, serum-albumin; the mucous glands, on the other hand, as their name implies, secrete a liquid free from albumin, but containing more or less mucin.

Fig. 9.

SECTION OF A MUCOUS GLAND (the submaxillary gland of the dog) showing the commencement of a duct in the alveoli (Schäfer, Quain's Anatomy, vol 2, p. 581).

a One of the Alveoli, several of which are in the section shown grouped around the commencement of the duct *d'*; *a'* an alveolus not opened by the section; *b*, basement membrane in section; *c*, interstical connective tissue of the gland; *d*, section of a duct which has passed away from the alveoli, and is now lined with characteristically striated columnar cells; *s*, semilunar group of darkly-stained cells at the periphery of an alveolus.

In the serous glands, the epithelium lining the acini is composed of comparatively small, rounded, or polygonal cells, of which the outlines are not very distinct until acted upon by certain reagents. No cell-wall is present; the protoplasm, which is not coloured by carmine, presents many dark granules, and surrounds an irregularly saccular or rounded nucleus which is coloured by carmine.

In the Mucous Glands (see Fig. 9) the characteristic (mucous) cells of the alveoli are large and clear, very faintly granular, with a rounded or oval nucleus near their periphery, surrounded by a trace of protoplasm. They possess a cell-wall, and a strongly refracting process which springs from the cell in the neighbourhood of the nucleus.

In addition to the characteristic mucous cells there are found in the alveoli of most mucous salivary glands when examined in a state of rest, situated at some parts of the periphery (see s, Fig. 9) *i.e.*, lying more external than, and nearer to the membrana propria than, the mucous cells, half-moon-shaped aggregations of small cells, possessed of a round nucleus easily stained with carmine, and containing much albumin; to these aggregations the term of *demilunes*, or *lunulæ* of *Gianuzzi* has been applied. In some cases we find alveoli in which these small cells are not arranged in demilunes, but form a row of cells lying external to the mucous cells, and completely encircling them.

As I have said, in certain mucous glands the mucous cells are supplemented by the cells of the demilunes, though certain mucous glands, as those of the tongue, exist where the typical mucous cells alone occur.

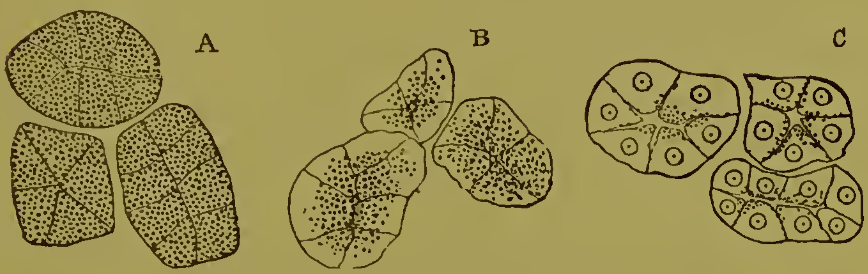
There are glands, and the submaxillary of man is an example, which are termed mixed glands, inasmuch as some of the acini have all the characters of serous, others of mucous glands.

The researches made during the last few years by Heidenhain, and fully confirmed and extended by Langley and other observers, have demonstrated that in the salivary glands, as indeed in the majority of secreting glands, structural and perfectly obvious microscopic changes occur, which stand in close relation to the different conditions of functional activity.

The resting gland cells may in the case of serous glands be shown to contain a large amount of granular matter (Fig. 10, A). The cells of glands which have been engaged in the act of secretion are found to have diminished in size, and to

have lost much of their granular matter (see Fig. 10 B and C), whilst the matter of the cell stains more easily than before.

Fig. 10



ALVEOLI OF SEROUS GLANDS.

A, at rest; B, after a short period of activity; C, after a prolonged period of activity (Langley).

The resting gland-cell is large, but possesses comparatively little matter which can be stained by colouring matters, especially by carmine; it contains, instead, a store of material which has been elaborated in, or at the expense of, the protoplasm. This material does not constitute the specific matter of the secretion, but is its antecedent. That it differs chemically in the case of the mucous glands is proved by the fact, cited by Heidenhain, and discovered by Watney and Klein, viz., that whilst *mucin* is stained by logwood, its antecedent (*mucigen*) is not affected by that colouring matter; in all other respects the two bodies are identical. When, however, a gland passes into a state of activity, the gland-cells undergo the following changes, which may proceed simultaneously though not necessarily so:—the stored up matter previously referred to is converted into soluble constituents of the secretion, and at the same time there occurs a growth of the protoplasm of the cells, at the expense doubtless of the richer supply of lymph which bathes the gland during the secretory act.

The period of activity is indeed, in so far as the gland-cell is concerned, a period of removal of ready-made constituents of secretion, and in some cases, as in the mucous-bearing cells of the mucous glands, a period of destruction of cells laden with such constituents; but at

the same time, in all cases, a period in which the protoplasmic constituents of the cells generally increase, and active proliferation of secreting cells occurs.

The Nerves which supply the Salivary Glands.

Each salivary gland is supplied by at least three classes of nerve fibres, viz., secretory fibres, vaso-constrictor and vaso-dilator fibres, of which the first and the third are conveyed to the glands in branches of cerebral nerves; these are, the chorda tympani for the submaxillary and sublingual and the auriculo-temporal (which, however, derives them through communications with the otic ganglion) for the parotid. The second class of vaso-constrictor or vaso-motor fibres run in sympathetic trunks. When, therefore, one of the cranial branches supplying a gland is stimulated, there occur two acts, viz., secretion and simultaneous dilatation of blood vessels; that these two acts are not absolutely interdependent is proved by the fact that certain drugs paralyze the one set of fibres, leaving the other intact. When, on the other hand, the sympathetic filaments supplying the gland are stimulated, the blood-vessels of the gland contract, and there is produced a small quantity of saliva differing in physical characters and chemical composition from that obtained under the circumstances first referred to. According to Heidenhain, however, in each of the two kinds of nerves supplying a salivary gland there exist, besides the vascular nerve-fibres, secretory and trophic fibres, though the number of one or other of these classes may be insignificant,—the secretory predominating in the cranial nerve branches, the trophic in the sympathetic. Stimulation of secretory fibres leads, according to Heidenhain, to an increased flow of water; stimulation of the trophic to an increased secretion of specific substances, and to an increased production of protoplasm.

When a salivary gland passes from the state of rest into that of activity it is at once the seat of an increased blood flow, which is associated with the dilatation of the blood-

vessels of the organ. Under these circumstances, the blood leaving the gland presents a florid arterial instead of a venous colour, which characterizes that of the organ when at rest. This vascular dilatation is explained by the coming into action of the before-mentioned vaso-dilator fibres; it is independent of the act of secretion

Heat evolved in the Salivary Glands.

As was shown in a now classical investigation of Ludwig, when the salivary glands are thrown into activity there is a rise in temperature, so that the temperature of the saliva leaving the submaxillary gland may exceed by $1^{\circ}\cdot 5$ C. that of the blood flowing to the gland. This rise in temperature cannot be explained by a study of the chemical characters of the salivary secretion, but is doubtless the result of the increased chemical changes which necessarily accompany the act of secretion in the gland-cells, and which chiefly affect their protoplasm.

The Function of Saliva not an act of Filtration.

That the secretion of saliva (and indeed secretion in general) is not a mere act of filtration was proved by Carl Ludwig, when he showed that saliva can be secreted by a gland though the pressure within it is many times higher than that of the blood circulating through the arteries which supply it. On many grounds it may be positively asserted that the secreting cells are the primary agents in the withdrawal from the blood of the water necessary for the secretion, though the exact nature of the process is yet unknown; similarly, on the grounds stated below, we know that within the protoplasm of the gland-cells are formed the characteristic soluble constituents of the secretion.

Quantity of Saliva secreted.

In the case of saliva, as in that of other digestive juices, we possess no mode of determining, in a reliable manner,

the amount of the secretion which is poured out in the physiological condition.

Wright calculated the daily secretion of mixed saliva at 10 or 12 ozs. Mitscherlich calculated the probable secretion to amount to 8 to 10 ozs. daily.

According to Tuczek, the salivary glands of an adult man secrete during mastication *at the rate of* 1300 grammes of saliva for each 100 grammes of gland-substance, the saliva containing 6·3 grammes of solid constituents, of which 3.9 grammes consist of organic matters.

Physical and Chemical Properties of Mixed Saliva.

Normal saliva is, when perfectly fresh, a clear, transparent, viscid fluid, which on microscopic examination is found to hold in suspension, but very sparsely distributed through it, cells of squamous epithelium, which have become detached from the walls of the mouth, besides certain cells denominated salivary corpuscles ; these cells, which present some resemblance to white blood corpuscles, are much more globular, and contain within their interior granules which exhibit in a very remarkable manner *Brownian* movements.

The specific gravity of the mixed saliva of man varies between 1·002 and 1·006, the mean being, however, about 1·003.

Perfectly normal human saliva possesses a faintly alkaline reaction, which is least marked after a long fast, and most distinct when the flow of the secrection is at its height. In some persons, especially in the morning, the saliva is found to possess an acid reaction, which is however due to fermentative changes.

Frerichs found that 100 grammes of saliva secreted by himself during smoking required 0·150 grammes of sulphuric acid to neutralize it.

The table to which I now direct your attention exhibits the results of analyses of the saliva made by the most reliable observers.

Results of Quantitative Analyses of mixed Human Saliva.

The following analyses exhibit the results obtained by Frerichs, Jacubowitsch, and Herter :

——	(1) Frerichs.	(2) Jacubowitsch	(3) Herter.
Water in 1000 parts. . . .	994·10	995·16	994·698
Solids	5·90	4·84	5·302
Soluble organic matters . . .	1·42	1·32	3·271
Epithelium	2·13	1·62	?
Potassium sulpho-cyanate . . .	0·10	0·06	?
Inorganic salts.	2·19	1·82	1·031

You observe how very abundant a constituent of the saliva is water, and that of the 5 or 6 parts of solid matters contained in 1000 parts of the mixture, about one half are organic matters and the other half mineral.

First let me dispose of the salts of the saliva. The chief of these are salts of sodium. It is a strange fact that the saliva always contains a soluble *sulpho-cyanate*, rendered evident by the red colouration which is shown when a little solution of a ferric salt is added. Among the saline constituents are traces of nitrites and some ammonia.

Passing next to the organic matters, we find that in largest quantity are suspended epithelium cells, which have been shed from the gland and passed into the secretion. Of the organic solids which are in a state of solution in the liquids, there are two which require our attention. The first of these is a body called *Mucin*, which is precipitated by acids, and which we find in many more or less viscid secretions, a body related to and unquestionably derived from the true albuminous substances of certain of the secreting cells. The mucin of the mixed saliva of man is mainly derived from the secretions of the submaxillary and sublingual glands.

The Diastatic Ferment.

The second and most important constituent is the *Diastatic Ferment*, sometimes called *Salivary Diastase* and also *Ptyalin.*

This, in many respects the most interesting constituent of the saliva, and which is invariably present in this secretion in man, is by no means a usual constituent of the saliva of the lower animals.

It was Leuchs who first ascertained that when human saliva is mixed with starch it gradually dissolves it, with the formation of a body which possesses the reactions of grape-sugar. Schwann confirmed this discovery, the truth of which soon received general assent, though the great majority of scientific men declared themselves of the opinion that in the living organism the saliva could not exert this action to an appreciable extent, and that its function depended essentially upon its watery character aiding gustation, mastication and deglutition.

In 1845, Mialhe discovered that when filtered human saliva is mixed with 5 or 6 times its weight of absolute alcohol, a small quantity of a flocculent body is deposited, which he collected and dried at the temperature of the air. This body he found to be insoluble in strong alcohol, but soluble in water and very weak alcohol. He discovered its remarkable property of converting boiled starch into sugar, and from the resemblance to, indeed the apparent identity with, the ferment which Payen and Persoz had lately separated from germinating barley, he applied to it the name of *Animal* or *Salivary Diastase.*

He announced that one part of this body was able to convert into sugar 2000 times its weight of starch.

Attempts to separate this ferment in a state of purity have failed, though we have succeeded in learning a great many facts relating to its properties, and the action which it exerts. To some of these facts I now wish to direct your attention.

Action of Saliva on Starch.

The body which we call starch $(C_{12}H_{20}O_{10})_n$ is an organic compound of carbon, hydrogen, and oxygen, which is formed in the interior of certain vegetable cells, and which occurs in the form of granules, differing somewhat in microscopic characters, according to the vegetable which yields it. These granules, which occur most abundantly in certain grains and roots, present an appearance under the microscope which indicates that they are composed of a large number of concentric layers.

When the starch grains are boiled in water they swell greatly, and we obtain so-called starch paste.

I have to tell you, that the salivary ferment, and therefore the saliva, is almost without any action on unboiled starch. When added, however, to starch paste, the action of saliva which, like human saliva, is rich in diastatic ferment is most striking.

In this beaker I have placed about a pint of a gelatinous solution containing potato starch. You observe how viscous is the solution as I pour it from one vessel to the other. I have taken the precaution of having the starch paste heated to about the temperature of the human body, and I now add a solution which contains some salivary ferment. You observe that almost instantly a great change comes over the gelatinous starch, which becomes perfectly limpid and transparent. The first action of the ferment is to convert gelatinous into soluble starch, that is into a body having the same reactions as insoluble starch. Like the latter body it strikes a beautiful blue colour with iodine, and is precipitated from its solutions by tannic acid and by alcohol.

But the production of soluble starch is only the first stage in the action of saliva. When the diastatic ferment acts for a longer time than suffices for the production of soluble starch, or when it is added in considerable quantities to starch paste, it is found that iodine no longer produces a

blue colour, but either a violet colour, or a red colour, or a more or less deep yellow colour, and lastly no perceptible colouration. The red colour produced by iodine is due to the production from starch of certain so-called *dextrins* characterised as *Erythrodextrins,* of which there are probably two distinct members. The yellow colour indicates the disappearance not only of soluble starch, but of erythro-dextrins, and the production of certain so-called achroo-dextrins.

All these dextrins are isomeric with, and are therefore represented by the same empirical formula as starch, though, as will be explained immediately, they are bodies of smaller molecular weight.

No sooner has the diastatic ferment commenced to act upon boiled starch, than we are able to detect in the solution the presence of a body belonging to the group of sugars, and this body was until lately supposed to be identical with grape-sugar. Its presence may be demonstrated by the following, amongst other, tests :

1. When the solution is treated with a drop of a solution of copper sulphate, and then with an excess of solution of caustic potash or soda, a deep blue liquid is obtained which, when boiled, deposits a yellowish red precipitate of anhydrous cuprous oxide. The same reaction is obtained with the reagent known as 'Fehling's Solution,' and which contains dissolved in water copper sulphate, an alkaline tartrate, and much sodium hydrate.

2. When boiled with an equal volume of a solution of potassium or sodium hydrate, a yellow amber colour is developed, which becomes darker in shade as the boiling is continued.

It is now known that the sugar produced by the influence of diastatic ferments upon starch is identical with that formed in the malting of barley, and to which the name of Maltose is given. Maltose is not isomeric with glucose, but with cane sugar. Its formula when crystallized is : $C_{12}H_{22}O_{11} \cdot H_2O$. The reducing power of maltose on cupric oxide is to that of glucose in the ratio of 61 : 100 ; it is not directly susceptible of the alcoholic fermentation.

In the first stages of the diastatic digestion of starch there are large quantities of dextrins and little maltose present, but as the action proceeds, the dextrins diminish and the maltose increases in amount.

We may form some idea of this process in the following manner. Let us conceive the molecule of starch to be made up of an aggregation of *n* molecules, each of which is represented by the empirical formula, $C_{12} H_{20} O_{10}$. There are some reasons for believing that the value of *n* is in the case of soluble starch 10. Now under the influence of the diastatic ferment this complex starch molecule combines with the elements of water, and the result is the production of a dextrin having a lower molecular weight than starch, together with a molecule of maltose ; thus :

$$\underbrace{(C_{12}H_{20}O_{10})10}_{\text{Soluble starch.}} + \underbrace{H_2O}_{\text{Water}} = \underbrace{(C_{12}H_{20}O_{10})9}_{\text{Erythro-dextrin } \alpha.} + \underbrace{C_{12}H_{22}O_{11}}_{\text{Maltose.}}$$

But this first dextrin, in the presence of diastatic ferment under suitable conditions again combines with the elements of water, thus :

$$\underbrace{(C_{12}H_{20}O_{10})9}_{\text{Erythro-dextrin } \alpha} + H_2O = \underbrace{(C_{12}H_{20}O_{10})8}_{\text{Erythro-dextrin } \beta} + \underbrace{C_{12}H_{22}O_{11}}_{\text{Maltose.}}$$

The newly formed dextrin, however, again combines with the elements of water, and successively there are produced dextrins of smaller molecular weight, until the final product of the diastatic digestion of starch may perhaps be represented by the equation.

$$10\ \underbrace{(C_{12}H_{20}O_{10})}_{\text{Starch.}} + 8\ \underbrace{H_2O}_{\text{Water.}} = \underbrace{(C_{12}H_{20}O_{10})_2}_{\text{Achroo-dextrin.}} + 8\ \underbrace{(C_{12}H_{22}O_{11})}_{\text{Maltose.}}$$

The action of salivary diastase on starch, like that of the other digestive ferments is affected remarkably by certain conditions, of which temperature is, perhaps, the most important. At the temperature of the body of warm-blooded animals it proceeds with great rapidity ; the limits of temperature highly favourable to the diastatic action being between 30°C. and 45°C. If the temperature be

however raised to between 60° C. and 70° C., the ferment is destroyed and all diastatic action arrested.

Although exerting an action similar to that of vegetable diastase, the salivary diastase is not identical with it, as is proved by the following facts ; the salivary diastase is killed by a temperature of 60°–70° C., whilst the vegetable diastase acts most potently at 60°, and is only killed by a temperature of 80° C. Again salicylic acid stops the action of vegetable diastase when present in the proportion of 0.05 per cent., whereas it must be present in the proportion of 1 per cent. to exert a similar action upon the salivary diastase.

Have the Different Salivary Glands Different Functions?

In physical properties and in chemical composition, the secretions of the different salivary glands present certain peculiarities, upon which the time at my disposal forbids me to dwell at length. Thus the '*parotid* saliva' is the most watery, and the least viscid, and contains an albuminous substance similar to serum-albumin ; and 'submaxillary' and 'sublingual' saliva are characterized by a greater proportion of solids, and by the presence of more viscid mucin.

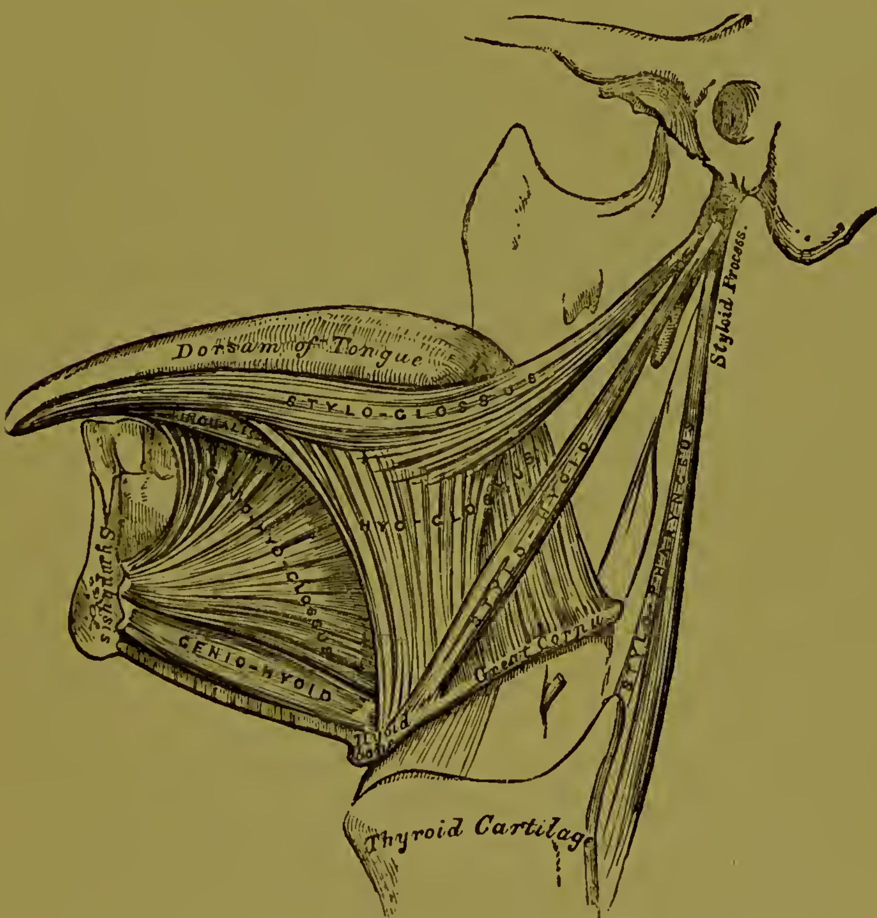
The great French physiologist, Claude Bernard, strove to establish a certain connection between the secretions of different salivary glands and certain functions. Thus, he showed that parotid saliva is, essentially and primarily, connected with the function of *mastication*, so that in those animals, as herbivores, in which mastication is a very elaborate and complex process, the salivary glands are most developed, and are larger in proportion to the other salivary glands. Similarly he showed that submaxillary saliva was connected more particularly with *gustation*, its secretion being stimulated by savoury food, or by mental emotions referring to food, whilst the secretion of parotid saliva accompanies the movements of the jaws.

The sublingual glands and saliva, he believed, though on less cogent grounds, to be subservient to the act of *Deglutition*.

Deglutition.

After the food has been reduced to a proper consistency by the combined influence of the mechanical movements of the jaws, tongue, and cheeks and the action of the saliva, it is rolled into a mass or *bolus* ready for swallowing. The bolus is pushed on the dorsum of the tongue, which is

Fig. 11.



THE MUSCLES OF THE TONGUE (GRAY'S ANATOMY).

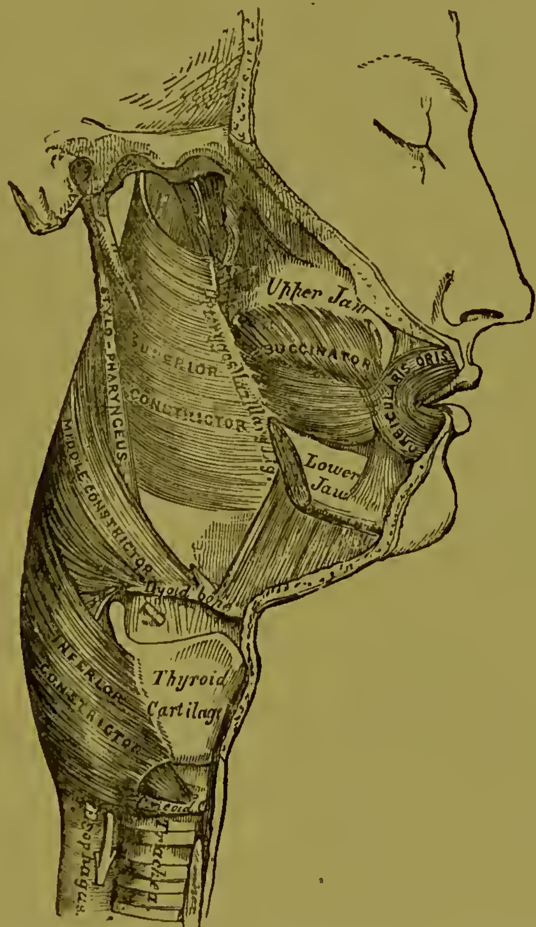
hollowed into a shallow trough to receive it. It is easy to conceive how this shape of the tongue is brought about when we consider that the tongue is provided with vertical fibres, with horizontal antero-posterior fibres, and with horizontal lateral fibres, in addition to its extrinsic muscles.

The tip of the tongue is then raised against the hard palate in such a manner as to form an angle in which the bolus lies. By the approximation of the tongue to the palate the angle is lessened and the bolus is, in consequence, driven backwards. This constitutes the first stage in the act of swallowing, and is a voluntary act. At the end of the first stage the morsel of food has passed beyond the level of the anterior pillars of the fauces. The acts of the second stage are very complicated, and probably are entirely involuntary. The posterior pillars of the fauces approach one another in the middle line, and the uvula falls into the space left between them. The fleshy curtain thus extemporised is then drawn up towards the hind wall of the pharynx, which is drawn a little forwards and upwards to meet it. Thus the passage into the nose is completely shut. Meanwhile the vocal cords of the larynx draw near to one another; the epiglottis is pushed backwards over the larynx, and the whole larynx is drawn suddenly upwards and forwards beneath the root of the tongue. In this manner the entrance into the respiratory passages is protected. Finally, the anterior pillars of the fauces are made to meet over the tongue in order to prevent the regurgitation of the food. There is but one way open to the bolus, the sudden drawing forward of the larynx and the base of the tongue in fact "cuts the ground" from under the ball of food, which thereupon falls into the grasp of the "constrictors" and enters upon the third and final stage in the act of deglutition. This, even more certainly than the second stage, is purely involuntary. The constrictors contract from above downwards and force the morsel of food into the upper portion of the œsophagus. Once in the gullet, the mass of food is driven downwards by the so-called "peristaltic" movements of the tube—the circular fibres contract one after another from above downwards, lessening the calibre of the tube in successive stages, whilst the longitudinal fibres seem to have the function of drawing the tube over the bolus as a stocking is drawn over the foot.

Deglutition is a reflex act, in so far as it is involuntary,

the centre for which lies in the medulla oblongata; destruction of this centre implies incapacity to swallow. The centre, though normally under the influence of the higher centres, may, however, act quite independently of these, as is evidenced by the fact that animals have occasionally

Fig. 12.



THE MUSCLES OF THE PHARYNX AND THE RELATIONS OF THE PHARYNX TO THE MOUTH, THE ŒSOPHAGUS, THE LARYNX AND TRACHEA (GRAY'S ANATOMY).

survived for a short time in which the cerebral hemispheres were absent, and have yet been able to suck and to swallow. Although the excised gullet often exhibits a true peristalsis, which doubtless depends upon a local nervous mechanism, the normal movements in the body seem to be regulated from the medulla oblongata. In curarised animals the

pneumogastric nerves seem to have some inhibitory influence over the movements of the gullet, as these become very active when the vagi are cut or the medulla oblongata is destroyed.

At the entrance of the stomach the food meets the barrier opposed by the contracted cardiac orifice; the contraction must be overcome before the food can gain admittance. The relaxation is certainly an active process under the control of the medulla oblongata through the vagus nerve, since section of the vagi causes a block to the progress of food from the œsophagus into the stomach.

LECTURE IV.

THE STRUCTURE OF THE STOMACH.—THE PROCESS OF SECRETION OF GASTRIC JUICE.—GASTRIC DIGESTION.

AT the conclusion of my last lecture I drew your attention very briefly to the process of deglutition or swallowing, which we saw was in part voluntary but mainly involuntary, and which has for its object the conveyance of the *bolus* of food from the cavity of the mouth through the *pharynx* into the œsophagus or gullet. I was compelled to pass over very briefly the remarkable combination of mechanisms by which the bolus in its passage through the pharnyx is prevented from entering either the nasal passages or the larynx and trachea.

The opening of the œsophagus into the stomach is guarded by a sort of sphincter, which is during life habitually closed, but which opens when food presses upon it, closing after its passage so as to prevent its return from the stomach. This sphincter is formed by a contraction of certain of the fibres of the muscular coat of the stomach specially developed with this object.

The Form and Relation of the Stomach.

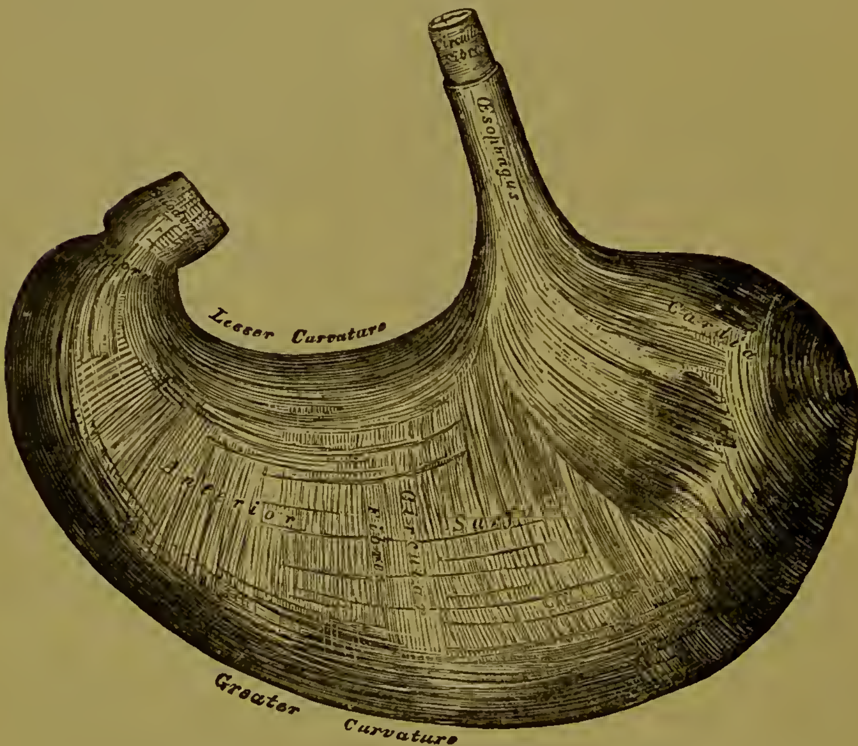
The stomach, as we have already seen, is a saccular dilatation of the alimentary canal situated between the œsophagus on the one hand, and the small intestine on the other (Fig. 13).

It is situated in the upper and anterior part of the abdominal cavity immediately behind its interior wall. It

occupies the region of the abdomen known as the left hypochondrium and the epigastric region.

The form, dimensions and position of the stomach vary according as it is empty or full.

Fig. 13.



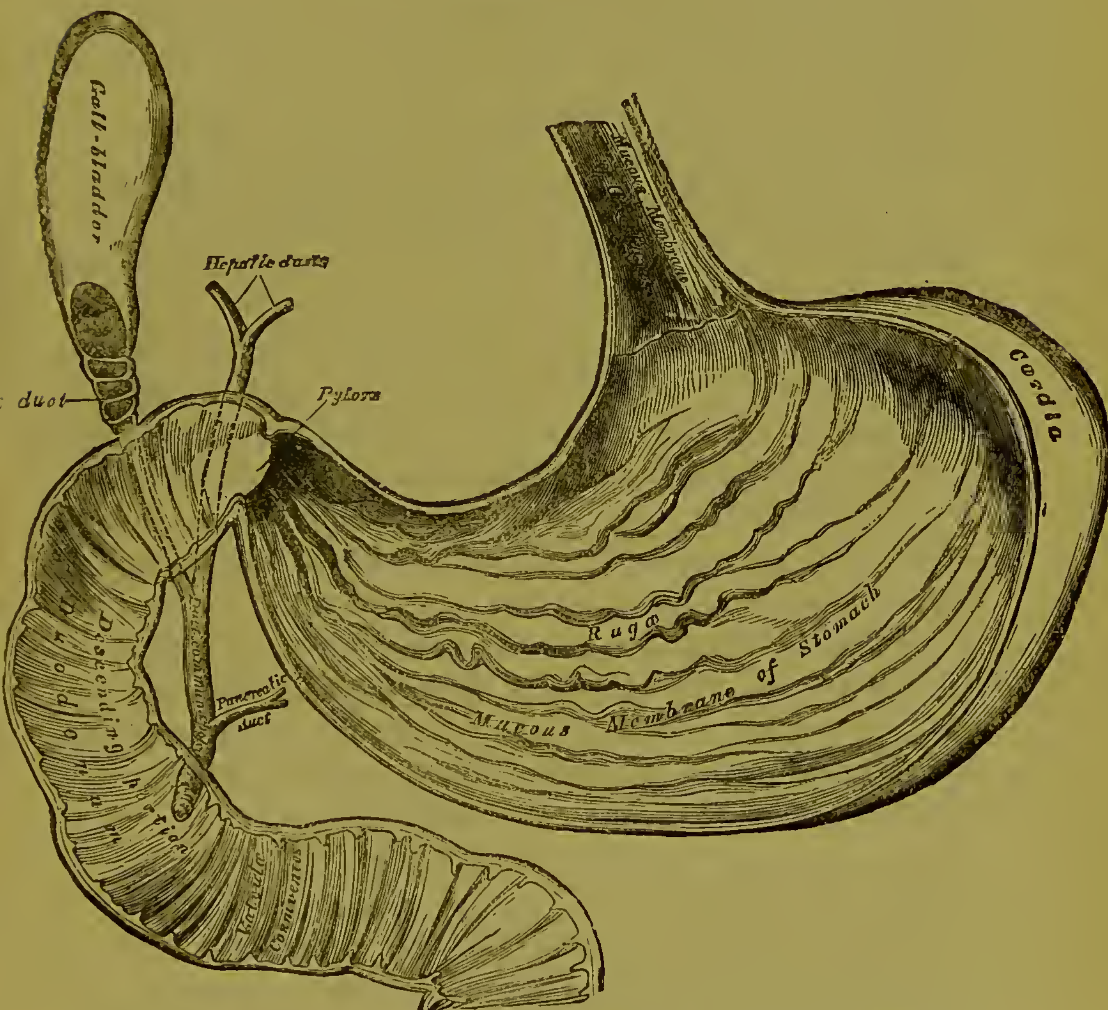
THE STOMACH WITH ITS PERITONEAL COAT REMOVED, EXHIBITING THE MUSCULAR COAT (GRAY'S ANATOMY).

"When moderately full it is about one foot in length, whilst its greatest transverse diameter is four to five inches.

"The general shape is pyriform, and it may be observed as possessing two extremities, two surfaces, and two borders (see Fig. 13). The larger extremity, called the *fundus*, *cardiac extremity*, or *great cul de sac*, is directed upwards so as to be in contact with the under surface of the diaphragm, whilst the smaller end, *pyloric* or *duodenal* extremity, is directed downwards, curves to the right, and becomes continuous with the duodenum. The *surfaces* form the *anterior* and *posterior* walls of the stomach. When the organ is empty the walls are flattened, and in apposition with each other by their inner surfaces; but when it is distended they are curved; the anterior convex surface, directed forwards and upwards, is in relation with the anterior abdominal wall,

the diaphragm and the under surface of the liver; the posterior surface, also convex, directed backwards and downwards, is in relation with the diaphragm, pancreas, transverse part of the duodenum, spleen, left kidney, and supra-renal capsule. The *borders* of the stomach are curved and unequal in size: one is

Fig 14.



THE INTERIOR OF THE STOMACH AND DUODENUM, WITH THE ENTRANCE INTO THE DUODENUM OF THE COMMON BILE DUCT AND THE PANCREATIC DUCT (GRAY'S ANATOMY).

convex, about three times as long as the other, and is named *the greater curvature;* the other is concave and forms the *lesser curvature.*

"The curvatures are so arranged that the greater has its convexity directed downwards and to the left, where it lies in relation to the transverse colon and the special flexure of the colon. The lesser curvature has its convexity directed upwards and to the right; for the

most part it is to the left side of the spinal column, with which it is almost parallel; it lies in relation to the cœliac axis.

"The œsophagus opens into the stomach at the upper end of the lesser curvature, and the cardiac orifice lies behind and opposite to the sternal fourth of the seventh left costal cartilage. Above this orifice the stomach expands into the fundus, which is situated in the highest part of the left hypochondrium, and occupies therefore the summit of the vault of the left half of the diaphragm. At the lower and right end the two curvatures lie almost horizontally in the epigastrium, and terminate at the pylorus, where the stomach becomes continuous with the duodenum.

"The pylorus, or gate of the stomach, is situated in the epigastrium about three fingers' breadth below the ensiform cartilage, and immediately to the right of the mesial plane. The junction of the stomach with the duodenum is marked by a circular constriction externally, called the *pyloric constriction*, and by a valve internally, the *pyloric valve*." *

The stomach is described as possessing four coats. Proceeding from without inwards, there are a *serous* or *peritoneal* coat, a *muscular* coat, a *cellular* or *submucous* coat, and most internally the *mucous coat* or *mucous membrane*, which lines the organ and which is continuous with that lining the remainder of the alimentary canal. I have only time to allude to the extreme smoothness of the glistening peritoneal coat, rendering perfectly easy all movements of the stomach in reference to contiguous viscera—a peritoneal coat which has the characters of all serous membranes, and which most superficially presents a single layer of flattened endothelial cells.

The *muscular* coat, of considerable thickness and of great physiological importance, is composed of sheets of unstriped involuntary muscular fibres arranged in two principal layers, an external longitudinal layer, and an internal circular layer, to which must be added an oblique layer chiefly developed at the cardiac end of the stomach.

The *submucous* or cellular coat is composed of connective tissue, and lodges the larger vessels and lymphatics and nerves and nerve-ganglia entering and issuing from the mucous membrane.

* 'An Introduction to Human Anatomy,' by William Turner, M.B. Edinburgh: Adam and Charles Black, 1877, p. 685.

Microscopic Structure of the Mucous Membrane of the Stomach.

The mucous membrane of the stomach is a thin membrane, presenting prominent folds, or *rugae*, most abundant at its pyloric end, and which disappear when the organ is distended. With a magnifying glass the mucous membrane is seen to present innumerable pits or *alveoli*, which are separated from one another by intervening ridges, at the bottom of which are the open mouths of the gastric glands, which are tubular glands, simple or compound, which occupy nearly the whole thickness of the mucous membrane.

In some animals, typically in the dog, the mucous membrane does not present one uniform appearance to the naked eye, nor is its structure identical in all parts. In the pyloric region it is less vascular, and appears thicker, though, as Heidenhain points out, it is here much poorer in glandular structures than at the fundus.

In the stomach of all animals there are observed two sets of glands, which formerly used almost invariably to be classified by English writers, as (*a*) peptic, and (*b*) mucous glands, to indicate the view, then held, that the first secreted gastric juice, whilst the second merely secreted mucus. In the dog, the former are absent from the pyloric region, but occupy the mucous membrane of the fundus and curvatures; they are therefore often spoken of as the *glands of the fundus.* On the other hand, the other glands are spoken of as the *pyloric glands.* In some animals where, as in the dog, these two structurally different regions of the stomach are observed, an intervening region, with transitional forms between these two sets of glands, has been described.

The whole mucous membrane of the stomach, with its depressed alveoli and the intervening ridges, is covered by cylindrical epithelium cells, similar to those of the intestinal tract. These epithelium cells are mucus-forming cells, and

amongst them we often observe, especially during digestion, mucus-secreting goblet-cells. The epithelial cells lie upon a basement membrane composed of apposed endothelium-like cells.

The Glands of the "Fundus."

At the fundus of the stomach the mucous membrane appears thinner, but it contains a far greater amount of glandular elements than are found in the pyloric region. The individual glands are deeper, and they are separated from one another by a much smaller quantity of connective tissue.

The Peptic glands (see Fig. 15), are usually arranged in groups of four or five. The open mouths at the bottom of the alveoli lead into ducts lined by cylindrical epithelium; "into each of these ducts open two or three tubes, the gland tubes proper."

In the gland tube we may distinguish, with Klein, a somewhat constricted *neck,* and a main part the *body*, which increases in width as it proceeds towards the blind extremity or *fundus.*

The gland tube possesses a *membrana propria*, or basement membrane, upon the inner surface of which is placed the secreting epithelium, and outside of which are blood-vessels, lymphatics and nerves.

It has been said, that the epithelium lining the duct common to several secreting tubes is columnar; in the glandular tubes themselves epithelium cells of two kinds are observed. Firstly, large ovoid granular cells, with oval nuclei, are seen lying against the basement membrane and causing it in some places to bulge outwards. These are the *peptic cells*, properly so called, of the older English writers, the *border cells* of some writers, the *delomorphous cells* of Rollet; they do not form a continuous layer, but occur at intervals.

Situated internal to them and between them are cylindrical or cubical cells, the so-called *adelomorphous cells* of Rollet, which have been called *principal cells* by Heidenhain,

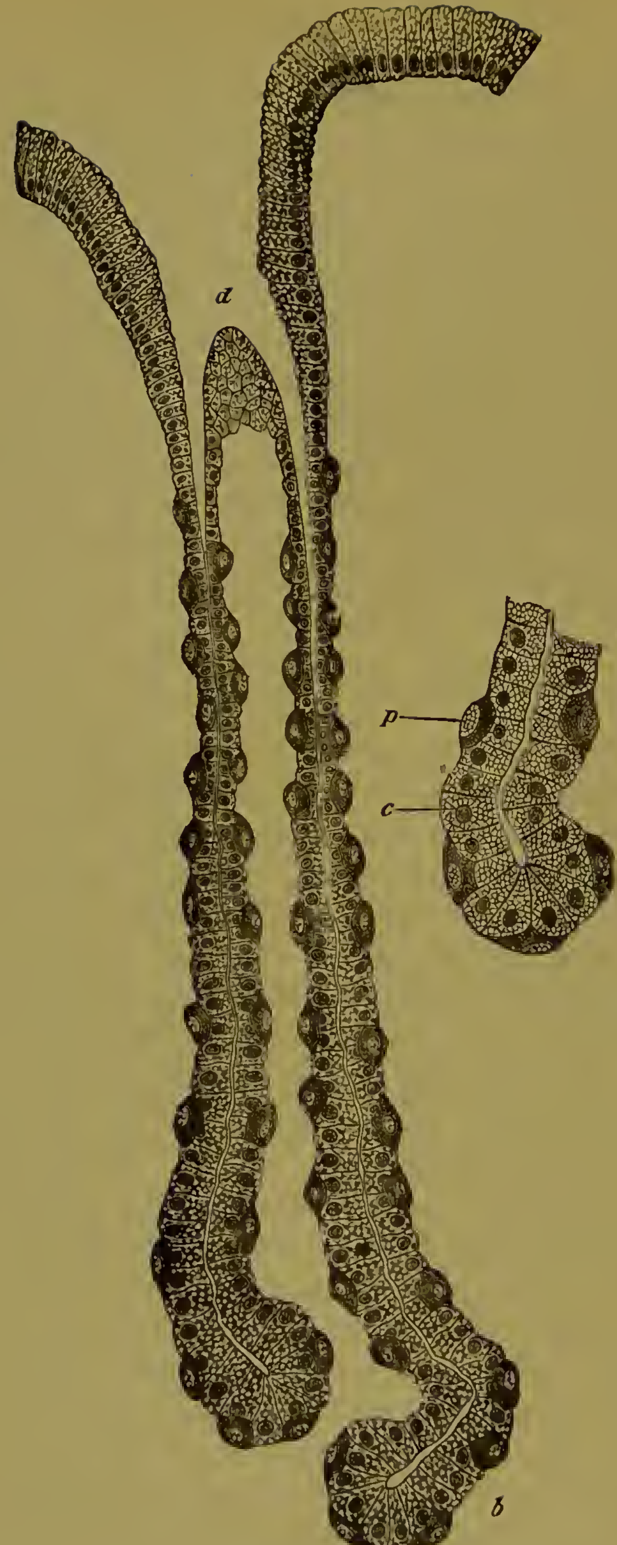
and which may most fitly be described as the *central* cells of the peptic glands. These central cells are recognised as essentially similar, both in structure and function, to the deeper columnar or more properly cubical cells which alone line the interior of the fundus of the pyloric glands. Heidenhain points out, however, that the principal cells of the peptic glands present a coarse granulation which hides the borders of the separate cells, whilst the cells of the pyloric glands contain a much finer granular matter which allows of their borders being distinctly seen. The lumen of the peptic glands is an exceedingly narrow canal, and contrasts with the much wider canal which penetrates to the depths of the pyloric glands.

The Pyloric Glands.

The characters of the pyloric gland (see Fig. 15) are thus summarized, and compared with those of the peptic glands, by Dr. Klein :—" The duct is proportionately very long ; it amounts to half or more of the whole length of the gland : two or three tubes open into the duct by a very short neck, which represents the narrowest part of the gland : the body of the gland is branched into two or three tubes, which are wavy and convoluted ; the lumen of the neck, but especially that of the body of the gland, is much larger than in the corresponding parts of the peptic gland ; the lumen in the body of the former glands being many times longer than that of the latter. The epithelium covering the surface of the mucosa and lining the ducts in the pyloric region is exactly the same as in the rest of the stomach. The epithelium lining the neck and body of these glands is a continuation of that of the duct ; but, as in the case of the peptic gland, so also here the cells are shorter and more opaque in the neck than in the body. In this latter the cells are fine, more or less transparent, columnar cells ; in no part are there parietal cells," &c.

As I shall tell you in the sequel, the product of the activity of the glands of the stomach is a peculiar liquid,

Fig. 15.



A CARDIAC GLAND FROM THE DOG'S STOMACH, HIGHLY MAGNIFIED (KLEIN AND NOBLE SMITH).

a duct or mouth of the gland ; *b* base or fundus of one of its tubules. On the right the base of the tubule more highly magnified ; *c* central cell ; *p* parietal cells.

the gastric juice—a liquid which may be looked upon as an aqueous solution of *hydrochloric acid* and of a ferment called *pepsin*. It has been conclusively proved that the latter body or perhaps an immediate precursor of it which we may term *pepsinogen*, is formed in part in the cubical cells which line the

Fig. 16.

A CARDIAC GLAND OF SIMPLE FORM, FROM THE BAT'S STOMACH (LANGLEY).

c columnar epithelium of the surface ; *n* neck of the gland, with central and parietal cells ; *f* base or fundus, occupied only by principal or central cells, which exhibit granules accumulated towards the interior of the gland (from *Quain's Anatomy*).

deeper parts of the pyloric glands, but chiefly in the central cells of the glands of the fundus. The acid of the gastric juice is, however, formed in the parietal ovoid cells of the glands of the fundus. You may therefore look upon these glands as the *oxyntic* (Langley) or acid-forming glands of the stomach, whilst we admit that the function of forming

the principal stomach ferment, *pepsin*, is shared by both the groups of gastric glands, though unquestionably the glands of the 'fundus' are much the more important.

An Historical Restrospect concerning Gastric Digestion.

As I have already hinted, the processes going on in the stomach are divisible into mechanical and chemical, it

Fig. 17.

A PYLORIC GLAND, FROM A SECTION OF A DOG'S STOMACH (EBSTEIN, TAKEN FROM QUAIN'S ANATOMY).

being well understood that *vital* apparatus contributes to the production of the physical and chemical conditions which are in operation. And firstly, let us confine our attention to the chemical or chemico-vital changes which

the food undergoes in the stomach. Our object must be to explain the changes which cause the merely broken down mixture of alimentary substances which enters the stomach to be partly dissolved and the remainder broken up further into the pulpy substance to which the term *chyme* has been applied. The agent effecting the changes which the food undergoes in the stomach is an acid fluid, termed the gastric juice, which is secreted by the gastric glands.

That the gastric juice is in reality the active agent in the digestive process of the stomach is proved by the following facts.

Firstly, the food is dissolved in the stomach when no other influence except that of the gastric juice can be exerted on it, and secondly, the food is dissolved by the gastric juice, even outside of the stomach, providing the temperature be sufficiently high.

Before entering into a minute account of the present state of our knowledge of the action of the gastric juice, it will be instructive to trace the more salient points in the history of the subject.

Many of the ancient physiologists held that the process of digestion was one of maceration, or as they termed it, *coction, i.e.* that the food was merely broken down under the combined influence of moisture and warmth. Again it was thought that digestion was merely a process of trituration; this was the result of false inference by analogy with the fowl's gizzard. Observers of the last century proved that it could not be mere trituration, but that the movements of the stomach merely aided the solvent action of the gastric juice. This conclusion was first arrived at in 1752 by the French naturalist Reaumur, who experimented on a tame buzzard, which, like the owl, hawk, &c., swallows its food and subsequently regurgitates the hairs and other undigested matters. He caused the buzzard to swallow food placed in little metallic tubes shut at one end and covered at the other by muslin, so as to preclude the possibility of the food being triturated and yet permitting the gastric juice to exert its solvent action.

He found that the food was dissolved in the tube. He ascertained that even bone became softened in it. He placed a piece of sponge in the tube, and introduced it into the stomach, and he obtained the sponge soaked with gastric juice.

After Reaumur, Dr. Stevens, in an Inaugural Thesis presented in 1777 to the University of Edinburgh, detailed some very curious experiments. He availed himself of the presence in Edinburgh of an Hungarian, who had the power of swallowing stones, and then regurgitating them. Stevens caused this man to swallow little silver balls with holes like a sieve, so constructed as to admit of being filled with food and closed by screwing. Dr. Stevens found that after these balls had sojourned in the stomach for some time their contents were dissolved. The same investigator also obtained the gastric juice of a dog, and observed that when placed in a warm locality it had the power of digesting meat.

Spallanzani, by experiments on fishes, reptiles and on himself, confirmed and extended the results previously arrived at by Reaumur and Stevens. We thus see that before the end of the last century the action of the gastric juice was tolerably well known, as well as its acid properties, and yet some persons doubted the accuracy of these results, stating that no acid fluid could be found in the stomach after death. They fell into error because they examined the stomachs of animals dying at a time when the stomach was not engaged in the process of digestion, and when therefore no gastric juice is to be found in it.

In 1800 Tiedeman and Gmelin carefully investigated the whole subject of digestion. They confirmed the observations of Reaumur, Stevens and Spallanzani, examined the chemical characters of the fluids secreted by the internal surface of the alimentary mucous membrane, and the changes effected by them on the food. Their researches embraced, indeed, the whole subject of digestion.

Then came some remarkable observations carried on by Dr. Beaumont, on a Canadian named Alexis St. Martin.

This man had, as the result of a gunshot wound, a permanent gastric fistula; that is to say, the cavity of his stomach communicated with the exterior by means of an opening situated on the left side of the chest two inches below the nipple. The borders of the opening into the stomach, which was of considerable size, had in healing united with the margins of the external wound, but the cavity of the stomach was separated from the exterior by a fold of mucous membrane which projected from the upper and back part of the opening, closing over it as a valve, but yet admitting of being pushed back.

Dr. Beaumont found that when the internal surface of the stomach was irritated mechanically, as by introducing the bulb of a thermometer into it, or when food entered the stomach, the mucous membrane became turgid, *i.e.* congested, and droplets of the acid gastric juice, began to ooze from its surface and trickle down. Introducing an elastic tube into the stomach he was enabled to draw off considerable quantities of gastric juice, and to cause it to act outside of the body, under varying conditions, upon the various alimentary substances. He had the opportunity of observing the influence of the bodily health, and of improper supply of food and drink (*e.g.* as intemperance), upon the aspect of, and secretion from, the gastric mucous membrane. He also made elaborate observations on the digestibility of various aliments, or rather on the rate with which various substances are converted into chyme.

Physical and Chemical Characters of the Gastric Juice.

Pure gastric juice is a thin, usually colourless though sometimes, as in the dog, yellowish liquid, possessed of a very acid reaction, and of a faintly acid mawkish taste, and of a peculiar though not easily defined odour.

It has a specific gravity, which varies between 1001 and 1010, the specific gravity varying in the same animal with varying conditions of the secretion.

When boiled, the gastric juice is not coagulable, but

ceases to be active. When cooled to 0° C. the gastric juice of warm-blooded animals ceases to exert its peculiar digestive powers.

The gastric juice of man contains less than 1 per cent. of solid matters, of which about two-thirds are organic, and one-third mineral.

The gastric juice may be kept for weeks and months without exhibiting any signs of putridity, and retaining its proteolytic activity. It possesses considerable antiseptic properties, as may be observed by moistening slightly putrid meat with the juice. This property has been ascribed to the free acid which it contains.

Its Essential Constituents.

The essential physiological attribute of the gastric juice is the power of breaking down and dissolving a large part of the solid proteid aliments, and ultimately converting them into *peptones*. This power depends upon the co-existence in the juice, of a ferment termed Pepsin and an acid which has been shown to be either free Hydrochloric acid or a more complex conjugated acid formed by the union of hydrochloric acid with an organic body, which, however, if it exists, is readily dissociated with the evolution of hydrochloric acid. Neither pepsin nor hydrochloric acid are active alone, but a mixture of the two bodies, in the presence of a proper quantity of water and at a suitable temperature, act essentially as the normal gastric juice. Whilst the enzyme pepsin is absolutely indispensable, the acid may be replaced by other acids, and yet proper digestion will take place.

Besides the proteolytic ferment pepsin, the gastric juice contains a *milk-curdling* ferment, which we may term the *Rennet ferment*. Neither pepsin nor the rennet ferment have yet been isolated as pure chemical bodies, but our knowledge of their properties is derived from a study of solutions which contain them in a state of more or less purity.

Besides the ferments we have mentioned, the gastric juice contains alkaline chlorides, earthy phosphates, and iron. No experiments have been made to determine the presence or nature of any gases which it may hold in solution or feeble combination.

Before considering in detail some of the facts which are known in reference to the ferments and the acid of the gastric juice and their relation to the process of digestion, let me draw your attention to a table exhibiting the composition of the gastric juice of the dog :

COMPOSITION OF THE GASTRIC JUICE OF THE DOG, OBTAINED WITHOUT ADMIXTURE WITH SALIVA (THE MEAN OF TEN ANALYSES BY C. SCHMIDT).

Water in 1000 parts	973·06
Organic matters (including peptones, pepsin, mecin)	17·127
Free HCl	3·050
NaCl	2·507
KCl	1·125
NH_4Cl	0·468
$CaCl_2$	0·624
$Ca_3, 2(PO_4)$	1·729
$Mg_3, 2(PO_4)$	0·226
$FePO_4$	0·082

Nature of the Acid of the Gastric Juice.

Some of the first chemists who investigated the nature of the acid of the gastric juice asserted that this was free hydrochloric acid, basing their conclusion upon the fact that when the gastric juice is distilled, free hydrochloric acid is given off from it. It was pointed out, however, that the acid obtained in this experiment might be the product of the action of some organic acid, such as lactic acid, upon an alkaline chloride.

The matter was well-nigh settled many years ago by C. Schmidt, when he pointed out that the gastric juice contains chlorine in greater amount than could exist in combination with the whole of the mineral bases present in the juice.

These results of Schmidt's have been confirmed by

Richet. There are, however, facts of another kind which support this view.

Mineral acids in general behave towards certain organic colouring matters in a different manner from organic acids. As a type of an organic colouring matter whose behaviour in presence of these two classes of acids is very characteristic, I shall cite one which is used as a dye and which is known as O O–Tropaeoline. I have an alcoholic solution of this substance, which, as you observe, presents the appearance of a brownish-yellow liquid. When I add a few drops to this very weak solution of hydrochloric acid, you observe the immediate development of a beautiful pink colour, whilst when I add a similar quantity to solutions containing much larger quantities of acetic acid or lactic acid, no such reaction is developed.

This and many other similar reactions bear out strongly the view that the acid of the gastric juice is a mineral acid —a view which is likewise supported by the fact that when the gastric juice is shaken up with ether, this fluid dissolves but infinitesimal traces of acid. Were the acid a free organic acid a different result would certainly be observed.

A view has been propounded within a comparatively recent time by M. Charles Richet, that the acid of the gastric juice is not free hydrochloric acid, but a conjugated acid or acid salt, in which hydrochloric acid is linked to an organic base, probably to *Leucine*.

Shortly after M. Richet's results were published, certain yet unpublished experiments made, at my request, and under my direction by one of my pupils (Dr. Haslam) convinced me that this view could not be held, as a solution containing hydrochlorate of leucine and pepsine possesses no power of digesting proteids.

Pepsin.

I have already referred again and again to the fact that the chief ferment of the gastric juice is a body called *Pepsin*, concerning whose action we know many facts,

though we have not succeeded in isolating it in a state of purity.

If we place the mucous membrane of the stomach of a recently killed animal, say of a pig, in glycerin for some days or weeks, the glycerin extracts the ferment, so that on mixing some of the solution with water and dilute hydrochloric acid, a fluid is obtained which possesses the essential property of the gastric juice. Other solvents, as, for instance, weak alcohol or sherry wine, likewise dissolve pepsin.

I have not time to describe to you the various methods which have been followed with the object of separating the pure ferment from the gastric juice and from the stomach. None of these methods have yielded a definite body. The most satisfactory has, however, furnished a product which enables us to say that pepsin is a proteolytic ferment of extraordinary activity, and that it does not belong to the group of albuminous or proteid bodies.

Artificial Gastric Juice and Artificial Digestion.

I have already told you that, in general, the glands which elaborate or prepare the digestive juices contain within themselves stores of the ferments characteristic of their secretions, or of bodies which are immediate precursors of the ferments—so-called *Zymogens.*

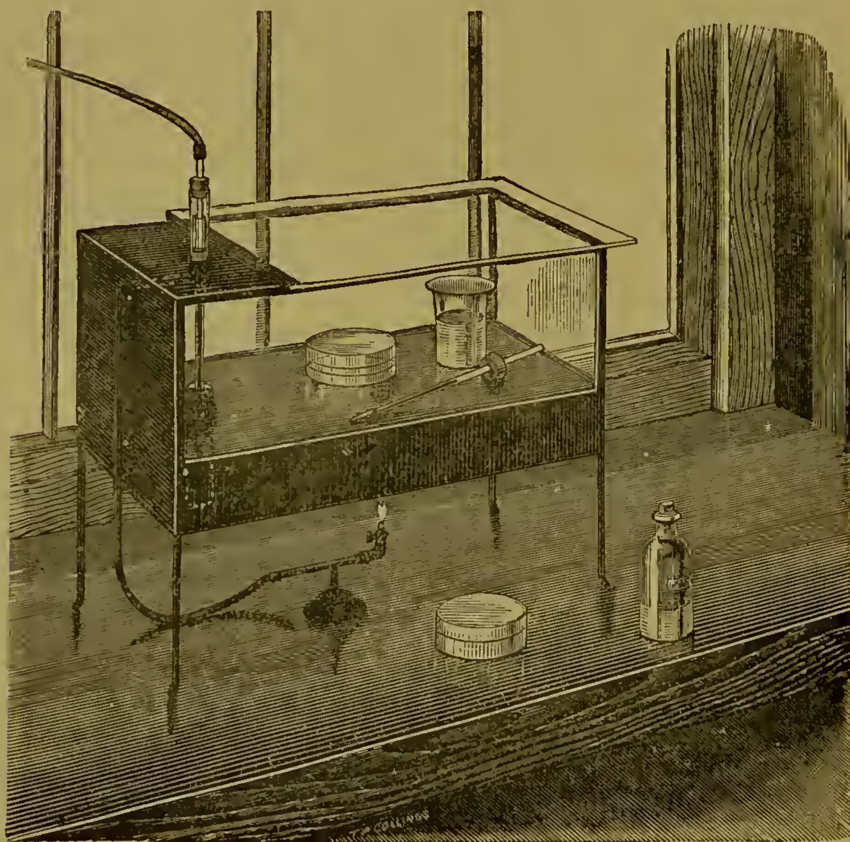
The glands of the mucous membrane of the stomach bear out these statements in a striking manner, as is proved by the fact just referred to, that glycerin or weak alcohol can dissolve pepsin from the mucous membrane.

When we place the mucous membrane of the stomach in water containing dilute hydrochloric acid and then raise the temperature of the mixture to the temperature of the mammalian body, the mucous membrane soon dissolves almost completely, and we obtain a liquid to which we give the name of *artificial gastric juice,* which will digest with ease in the same manner as the natural gastric juice. The acid to be employed in such experiments should contain

between 0·1 and 0·2 per cent of pure hydrochloric acid. (HCl).

Artificial digestions are usually conducted in water baths, or closets heated by hot water, so-called *Incubators*, provided with arrangements whereby a nearly constant temperature is maintained. Such an incubater is shown in Fig. 18.

Fig. 18.



AN INCUBATOR, OR CHAMBER SUITABLE FOR ARTIFICIAL DIGESTION.

The lower part of the chamber is filled with water. The supply of gas to the jet below is kept nearly constant by means of Page's mercurial regulator (Schäfer's *Practical Histology*).

With the aid of such an apparatus we may experiment satisfactorily. I have here three beakers, and into one of these I place some water containing 0·2 per cent of hydrochloric acid; in a second, water to which I have added

some glycerin-solution of pepsin; in a third a mixture of acidified water and pepsin.

The three beakers I place in the incubator and into each I now drop a fragment of well washed blood fibrin. If we examine the beakers in the space of an hour, we shall find that the fibrin placed in the first beaker (containing dilute HCl) has swelled and become exceedingly transparent; that the fibrin placed in the second beaker (containing pepsin) appears unaltered; whilst the fibrin placed in a mixture of acid and pepsin has completely dissolved.

Without pepsin, it is impossible to obtain an artificial gastric juice. Is the hydrochloric acid equally indispensable, or may it be replaced by some other acid? The answer is that whilst hydrochloric acid acts most efficiently, other acids may, in combination with pepsin and water, enable the ferment to act. An acid *reaction* is, however, not sufficient to allow pepsin to digest proteids; the acid reaction must be due to a *free* acid.

If we boil our artificial gastric juice, we find that it at once loses its activity, in consequence of the pepsin, like all other animal ferments, being destroyed by so high a temperature. Many powerful chemical agents which precipitate or decompose pepsin exert a similar destructive influence upon the digestive activity of artificial gastric juice.

Peptones, the ultimate Products of the Action of Gastric Juice on Proteids.

Gastric juice, natural or artificial, exerts no action upon starches, sugars, or fats. Its digestive power is limited to its action on the proteid or albuminous substances, represented by such bodies as egg albumin, blood albumin, myosin (the chief albuminous constituents of flesh), casein, &c., and upon the so-called albuminoid bodies, which are very closely related to the last, and which are represented chiefly by collagen and gelatin.

Under the influence of the pepsin and acid of the gastric

juice, the albuminous substances, whether originally soluble or not, are *ultimately* converted into highly soluble bodies called *Peptones*, though many intermediate products are formed, to some of which I shall refer when pointing out to you the special characteristics of the pancreatic digestion of proteids.

The Characters of Peptones.

Peptones, like the bodies from which they are divided, are proteids, or at least are most closely connected with the proteids. By ultimate organic analysis they are found to have the same elementary composition as the bodies from which they are obtained.

They possess, however, certain properties which distinguish them from all other proteids.

In the first place, the peptones are *exceedingly* soluble in water, and in this respect contrast with all other albuminous substances which are soluble in water (save hemialbumose).

In the second place, their watery solutions are not coagulated by heat, nor by the addition of any of the mineral acids, nor by neutralizing their solution if acid or alkaline.

Particularly, they are not precipitated by acetic acid and ferro-cyanide of potassium, which induces the precipitation of any other proteids in solution.

They are precipitated, however, by solution of tannic acid, and by solutions of phospho-molybdates.

When a solution of peptones is treated with a drop of a very weak solution of cupric sulphate and then caustic soda is added, a very pretty pink or rose colour is developed, whilst with other proteids, a violet colour is obtained. This reaction is, however, shared by one of intermediate products, to which we give the name of Hemi-Albumose.

The one property of great physiological importance which peptones possess is, however, that of *diffusing*

through animal membranes more readily than any other proteids. You remember that Graham pointed out that we may subdivide substances which are soluble in water into two groups, according to their power of diffusing through animal and vegetable membranes. If, for instance, I take a certain length of the empty intestine of an animal, and tie one end of it, I obtain a tube with walls composed of an animal membrane. Into this tube I pour a solution containing gelatin and common salt dissolved in water. Having introduced the solution, I apply a ligature to the tube a few inches above the level of the liquid, and hang the half-filled membranous tube in a jar holding distilled water. In a few hours I shall apply two tests to two different portions of the water. A solution of nitrate of silver will throw down a dense white precipitate of chloride of silver insoluble in nitric acid, showing that much common salt has made its way from the inside of the intestine, through its membranous walls, into the distilled water. To another portion of the water I shall add a solution of tannic acid, which possesses, as I now show you, the power of producing dense precipitates when added to solutions of gelatin. I shall find, however, that no gelatin will have diffused.

Graham called the bodies which are highly diffusible, "*Crystalloids*," for amongst the most highly diffusible bodies are many crystalline bodies : whilst he gave the name of "*Colloids*" to the bodies which like glue have little or no power of diffusing. Physiological chemistry teaches us that a body may be capable of crystallizing with ease, and yet be a colloid—such is the case with the beautiful crystalline Oxy-Hæmoglobin, the blood colouring matter,—and also, that bodies which have the closest relationship with, and which share, many of the properties of typical colloids, may be somewhat diffusible. Such are the peptones which we are now considering. It is true that their power of diffusing through the so-called "*parchment paper*" ordinarily employed in making the "dialysers" used in these experiments, is but small ; they have, however, a much

greater power of making their way through animal membranes.

By the action of the gastric juice, then, or of pepsin and hydrochloric acid, acting upon proteids, soluble or insoluble, under favourable conditions of temperature, there are ultimately produced highly soluble bodies—the *peptones*, which being diffusible, may pass through the walls of lymphatics and blood-vessels and thus enter the blood.

These peptones are, doubtless, bodies of simpler molecular weight than the albuminous substances which yield them, and their production is due to a splitting up of a complex into simpler molecules. It is, however, unquestionable, that from the peptones absorbed from the alimentary canal, the more complex proteid molecules again arise, by synthetic processes whose exact seat is not known. Of the fact, however, we are certain, seeing that we may for long periods substitute peptones for native proteids in the diet of an animal, without any perceptible difference in the nutritive condition of the creature.

The Milk-Curdling or Rennet-Ferment of the Stomach.

It has long been known that the mucous membrane of the fourth or true stomach of the calf possesses the property of curdling milk, and various preparations of this mucous membrane have, under the name of "rennet," been employed to coagulate casein in the manufacture of cheese. It has also long been known that the gastric juice curdles milk; this action has been ascribed by some to pepsin, and by others with greater justice to the free acid of the gastric juice.

It was, however, first shown by Heintz, that the mucous membrane of the stomach possesses the property of curdling milk when the reaction is neutral, and even alkaline. The recent researches of Hammarsten have demonstrated that the milk-curdling property depends upon the presence of an enzyme of which the zymogen is

often, though not invariably, present in the gastric mucous membrane.

The mucous membrane of the stomach of the calf and of the sheep always contains *ready-formed* milk-curdling ferment, which can be extracted from it by the action of water and other solvents to be mentioned hereafter ; most frequently none can be extracted by water from the mucous membrane of the stomach of other mammals or of birds, and it is scarcely ever present in that of fishes.

Although the free ferment removable by water is rarely found, Hammarsten has shown *that the gastric mucous membrane of all animals, without exception, in which it has been investigated, contains a body which is not the milk-curdling ferment, but from which the milk-curdling ferment is quickly liberated on the addition of an acid.*

Hammarsten has found that the mucous membrane of the fundus is very much richer in the milk-curdling ferment and its zymogen than that of the pylorus.

Although the mucous membrane of the stomach of the calf and of the sheep always yields to water having a neutral reaction a sufficient quantity of milk-curdling ferment to demonstrate its peculiar properties, much more powerfully-acting solutions are obtained by the aid of dilute acids, as follows :—The mucous membrane of the stomach, preferably of a calf, is digested for twenty-four hours, at ordinary temperatures, in 150—200 c.c. of very dilute hydrochloric acid, containing from 0·1 to 0·2 per cent. of HCl. The liquid is then filtered and carefully neutralized. Twenty-five c.c. of fresh milk are then heated to 38° C., and treated with 1 c.c. of the neutralized liquid. Curdling is induced within a period of two minutes ; this occurs even if the milk have been rendered faintly alkaline by caustic soda ; the alkaline reaction persists after curdling. A glycerin-extract of the stomach of the calf may be used, as Hammarsten first showed, instead of the solution prepared as stated above ; such a glycerin-extract can be preserved permanently, and is very active. Erlenmeyer has shown that a saturated aqueous solution of salicylic acid extracts

the milk-curdling ferment very perfectly from the stomach of the calf; from the solution the ferment mixed with other matters can be precipitated by alcohol. The precipitate thus obtained is soluble, in great part, in water, and the solution is active.

The ferment acts upon casein in neutral, acid, and feebly alkaline solutions, though an alkaline reaction diminishes, and, if marked, prevents curdling. The process of curdling is most rapidly brought about by solutions which have an acid reaction, which must not, however, depend upon a quantity of acid sufficiently large to precipitate, by itself, the casein.

The products of the action of the curdling ferment upon casein is different from the product of the action of acids; in the former case cheese is precipitated, in the latter casein.

The milk-curdling ferment does not convert milk-sugar into lactic acid.

Hammarsten precipitated a glycerin-extract of calf's stomach with alcohol, and dissolved the precipitate in water. The amount of dissolved matter was then determined, and also its power of coagulating casein. Assuming all the dissolved substance to consist of pure ferment, it would curdle from 400,000 to 800,000 times its weight of casein.

THE PROCESS OF DIGESTION IN THE LIVING STOMACH.

Having now spoken of the chemical composition of the gastric juice, the character of its separate constituents, and the action which they exert upon the particular class of proximate principles which are acted upon in the stomach, it remains to consider the actual process of digestion as it occurs in the living organ, and in doing so we shall be brought face to face with certain questions which have not been discussed in the preceding sections. Although experiments on artificial digestion teach us the nature of

the process which occurs in the stomach, we cannot pretend that such experiments will furnish us with data which will apply exactly to the stomach, for in this organ we have conditions which are very different from those which exist *in vitro.* In the stomach we have not an ordinary receptacle into which artificial gastric juice is poured so as to be mixed with food, but a receptacle kept constantly at a temperature most favourable to digestion, and provided with an arrangement for continually mixing the food to be dissolved with the solvent juice ; a receptacle, too, in which absorption of water holding certain substances in solution is continually going on, and secretion of the pepsin and acid needed to carry on the digestive process ; a receptacle from which, at a certain period of digestion, the more finely subdivided matter is gradually drawn off, leaving the grosser masses to be further subjected to the combined influence of mechanical movements and the solvent action of gastric juice. But for the continual removal by absorption of the peptones, which result from gastric digestion, the process would, as experiments on artificial digestion conclusively prove, quickly come to an end, only to recommence on further dilution of the liquid.

General Sketch of Digestion in the Living Stomach.

When food is introduced into the living stomach, the mucous membrane which was previously pallid becomes injected ; droplets of liquid commence to exude from the open mouths of the gastric glands, and, uniting, form a stream of gastric juice. At the same time the organ contracts around the mass which it contains, and complex movements occur which cause "not only a constant disturbance or churning of the contents of the organ, but compel them at the same time, to revolve around the interior from point to point and from one extremity to the other."

"When food first enters the stomach the movements are

feeble and slight, but as digestion goes on they become more and more vigorous, giving rise to a sort of churning within the stomach, the food travelling from the cardiac orifice along the greater curvature to the pylorus, and returning by the lesser curvature, while at the same time subsidiary currents tend to carry the food which has been passing close to the mucous membrane towards the middle of the stomach, and *vice versâ*."

"While these revolutions of the contents of the stomach are progressing, the trituration or agitation is also going on. There is a perfect admixture of the whole ingesta, during the period of alimentation and chymification. There is nothing of the distinct lines of separation between old and new food, and peculiar central or peripheral situation of crude, as distinguished from chymified aliment, said to have been observed by Philip, Magendie, and others in their experiments on dogs and rabbits, to be seen in the human stomach; at least in that of the subject of these experiments. The whole contents of the stomach, until chymification be nearly complete, exhibit a heterogeneous mass of solids and fluids; hard and soft; coarse and fine; crude and chymified; all intimately mixed, and circulating promiscuously through the gastric cavity, like the mixed contents of a closed vessel, gently agitated or turned in the hand." . . . . "As the food becomes more and more changed from its crude to its chymified state, the acidity of the gastric fluids is considerably increased, and the general contractile force of the muscles of the stomach is augmented in every direction; giving the contained fluids an impulse towards the pylorus. It is probable that from the very commencement of chymification—from the time that food is received into the stomach until that organ becomes empty—portions of chyme are constantly passing into the duodenum through the pyloric orifice, as the mass is presented at each successive revolution. I infer this from the fact that the volume is constantly decreasing. This decrease of volume, however, is slow at first; but is rapidly accelerated towards the conclusion of digestion, when the

whole mass becomes more or less chymified. This accelerated expulsion appears to be effected by a peculiar action of the transverse muscles, or rather of the *transverse band* . . . . . situated near the commencement of the more conical shaped part of the pyloric extremity, three or four inches from the smaller end. In attempting to pass a long glass thermometer tube through the aperture into the pyloric portion of the stomach, during the latter stages of digestion, a forcible contraction is first perceived at this point, and the bulb is stopped. In a short time, there is a gentle relaxation, when the bulb passes without difficulty, and appears to be drawn, quite forcibly, for three or four inches, towards the pyloric end. It is then released, and forced back, or suffered to rise again ; at the same time giving to the tube a circular, or rather spiral motion, and frequently revolving it completely over. These motions are distinctly indicated, and strongly felt, in holding the end of the tube between the thumb and finger ; and it requires a pretty forcible grasp to prevent it from slipping from the hand, and being drawn suddenly down to the pyloric extremity. When the tube is left to its own direction, at these periods of contraction, it is drawn in, nearly its whole length, to the depth of ten inches : and when drawn back, requires considerable force, and gives to the fingers the sensation of a strong *suction*-power, like drawing the piston from an exhausted tube. . . . . . These peculiar motions and contractions continue until the stomach is perfectly empty and not a particle of the food or chyme remains ; when all becomes quiescent again. . . . The peculiar contractions and relaxations, mentioned above, succeed each other at regular intervals of from two to four or five minutes. Simultaneously with the contractions there is a general shortening of the fibres of the stomach. This organ contracts upon itself in every direction ; and its contents are compressed with much force. . . . . . During the intervals of relaxation, the rugae perform their vermicular actions, the undulatory motions of the fluids continue, and the alimentary and chymous masses appear,

revolving as before, promiscuously mixed, through the splenic and cardiac portions."*

In quoting *verbatim* considerable portions of Dr. Beaumont's vivid and unique observations on his patient St. Martin, I do so because the description will give you some idea of the intensity of the mechanical movements which aid the chemical action of the gastric juice so efficiently as to enable the stomach to effect digestive operations which, in point of magnitude, cannot be imitated in the laboratory.

The term Chyme (χυμος juice) is generally applied to the pulpy semi-fluid matter resulting from the action of the gastric juice on the mixed aliments, and the term Chymification to the process which results in the formation of chyme.

When much fluid is introduced into the stomach, absorption at once commences actively. This is proved by the fact, amongst others, that almost instantly the sensation of thirst, when that exists, which depends primarily upon a diminution of the water of the blood, diminishes. At the same time, doubtless, the absorption of some diffusible substances occurs, as is proved by the fact that a few minutes after the introduction of potassium iodide into the stomach, the salt is separated by the kidneys and other glands. The extent to which the process of absorption proceeds in the stomach cannot, however, be exactly stated.

The constituents which are chemically acted upon by the gastric juice in the stomach are firstly the proteids, and secondly the *albuminoid* bodies, such as collagen and gelatin, chondrigen and chondrin.

The other groups of organic food constituents, viz. fats and carbohydrates, are very slightly acted upon by the gastric juice itself; in considering this slight action of the gastric juice we shall have to enquire to what extent the

* Beaumont, 'Experiments and Observations on the Gastric Juice.' Edinburgh edition, 1838, p. 101.

amylolytic action of the saliva upon the alimentary starch is allowed to proceed in the presence of the acid juices of the stomach.

The Changes which Adipose Tissue undergoes in the Stomach.

Until lately the majority of authorities have held that the fatty constituents of the food undergo no change in the stomach, although their subsequent digestion in the small intestine is promoted by the solution of the walls of the fat cells, which occurs in the stomach, and which liberates their fatty contents.

It was stated by Dr. Marcet, however, that a certain decomposition of the neutral fats takes place in the stomach, and in a recent research Dr. Cash has found that when dogs are fed upon perfectly neutral fats, fatty acids are liberated in small quantities, and that when the mucous membrane of the stomach is digested with neutral fats, in the presence of hydrochloric acid, fatty acids are likewise liberated. This setting free of traces of fatty acids will doubtless aid the subsequent emulsionizing of the fats by the bile and pancreatic juice.

The Changes which Starch undergoes in the Stomach.

In discussing the changes which starch undergoes in the stomach, we have to consider, firstly, whether the gastric juice possesses by itself any action upon starch, and secondly to what extent the action of the saliva upon starch continues in the stomach.

The saliva of many animals, *e.g.* the dog, is devoid of diastatic properties. If a dog be fed upon a meal of boiled starch and killed during digestion whilst the stomach still contains food, mere traces of sugar are found, but the contents contain both soluble starch and erythrodextrin (Brücke). Unboiled starch is unacted upon.

The contents of the stomach of man fed upon a diet containing boiled starch always contain considerable quantities of sugar, and the question arises, Was the sugar produced by the momentary action of saliva upon starch during mastication and deglutition, or did the conversion of sugar under the influence of saliva continue in the stomach ? In endeavouring to solve this question, we have to bear in mind, firstly, that diastatic ferments do exert their action upon starch in a fluid of *feebly* acid reaction, and, secondly, that that action is arrested so soon as the reaction becomes *strongly* acid. It would therefore appear most likely that in the early stages of gastric digestion, before the admixture with gastric juice is complete and when the acidity of the gastric juice is comparatively feeble, the diastatic action of the saliva proceeds in the stomach, whereas soon after, when the acid reaction has attained a certain amount, diastatic action diminishes or even ceases altogether.

The statements of various authors concerning the influence of an acid reaction upon the diastatic action of the salivary ferment differ remarkably. Thus Brücke asserts that in a solution containing 0·5 of HCl per 1000, the conversion of starch into sugar goes on, whilst when the quantity reaches 1 per 1000, no action on starch occurs Hammarsten found that the diastatic action ceased when the quantity of hydrochloric acid amounted to from 0·05—0·25 per cent. Langley observed that when saliva is digested with HCl of from 0·2 to 0·04 per cent. for times varying from twenty-four to seven hours the ferment was destroyed. On the other hand, Richet asserts that saliva exerts a more powerful action on starch in the presence of 2 parts per 1000 of hydrochloric acid, than when the reaction is neutral or feebly alkaline, and Defresne contends that diastatic action goes on unimpeded by the gastric juice.

Closely connected with the question just discussed is that whether the diastatic ferment is destroyed or not in the stomach. Upon this matter the statements of authors differ very greatly. Thus it is said by Cohnheim, that the diastatic ferment is not destroyed when submitted to

artificial digestion with pepsin and hydrochloric acid for many hours, for on neutralising the liquid it was found to possess diastatic powers. Schiff makes the same statement; and more recently Defresne has repeated it. Roberts, on the other hand, asserts that the diastatic power of the saliva is quickly and permanently abolished both by an artificial digestive fluid and by filtered gastric juice obtained from the human stomach. I have convinced myself of the accuracy of this statement, which is further confirmed by Langley.

Changes in the Acidity of the Contents of the Stomach during Digestion.

It has been already said that the acidity of the contents of the stomach increases as digestion proceeds, and attention must now be directed to variations which occur simultaneously in the nature of the free acid.

It has been shown in a previous section that the acid reaction of the gastric juice is due to the presence of free hydrochloric acid, though Richet maintains, of hydrochloric acid in combination with an organic body, such as leucine. V. der Velden asserts that in the first stages of digestion in the human stomach no free hydrochloric acid is present, as long as two hours elapsing after a full meal, such as dinner, before the acid appears.

The gastric juice behaves, it was shown, when shaken with ether, as an aqueous solution containing a mineral acid.

The pure gastric juice of man has an acidity which, according to Richet's observations, corresponds to 1·3 parts by weight of HCl in 1000.

When digestion is proceeding, however, the acidity increases somewhat. However large the quantity of liquid in the stomach, it is found to have an acidity which on an average (according to Richet) corresponds to 1·7 parts of HCl per 1000, though it may, especially at the end of digestion, exceed this figure somewhat. After the in-

gestion of acids or of alkalies, the normal acidity is soon re-established.

Richet has found that in the advanced stages of digestion the acidity of the contents of the stomach no longer depends solely on a mineral acid, but that considerable quantities of acids soluble in ether are present. These acids are in part produced by the decomposition of salts of organic acids present in the ingested food, but, according to Richet, in no small degree they result from acid fermentations which occur in the stomach. Thus in the digestion of milk, according to Richet, there is set up, as a normal process, an acid fermentation which leads to the development of large quantities of lactic acid. The feebler the normal acidity of the gastric juice, the greater the quantity of the organic acids resulting from fermentative changes. There can be no doubt that the acids thus set free reinforce the normal acid and co-operate in the process of digestion.

Duration of the Digestive Process in the Stomach.

The digestive process varies in duration in different animals, and in the same animal according to the nature of the food, its state of division, &c. Dr. Beaumont found the duration of the gastric digestive process in Alexis St. Martin, to be between three to five hours, and Richet remarks, as the result of his observations on his patient Marcelin, that the digestive process does not appear to extend beyond four or five hours.

In dogs and other carnivorous animals which are in the habit of "bolting" large masses of meat, undigested masses are found in the stomach eight or ten hours after a meal, and often longer.

The Final Products of Digestion which leave the Stomach. The Chyme.

As a result of the combined influence of the gastric juice, of the movements of the stomach and the high temperature

of the organ, the solid alimentary matters are reduced to a pulpy or semi-fluid condition, and it is in this state that they are allowed to escape through the pylorus into the duodenum.

During the digestive process large quantities of proteids and of albuminoid bodies have been converted into peptones, of which doubtless a part—though we have no data on the subject—is absorbed by the gastric mucous membrane as soon as formed, whilst a part is held in solution in the liquid portion of the *chyme*. As a result of the action of the acid of the gastric juice, insoluble mineral salts, as *e.g.* bone-earth, are dissolved and doubtless are absorbed, as are also soluble salts, sugar, and large quantities of water.

The chyme, then, must contain chiefly the undigested or partially digested fragments of food, mixed with gastric juice holding products of digestion in solution.

Accordingly, we observe it to contain fragments of muscle, and individual muscular fibres splitting into fibrils, and tending to cleave into transverse discs. The fibrillar connective tissue has wholly or in great part disappeared, but yellow elastic tissue is found apparently quite intact; the same remark applies to cellulose and to the epidermal tissues of animals. If raw starch has been partaken of, the chyme is sure to contain unaltered starch grains.

Lastly, if adipose tissue or any fat was contained in the food, drops of liquid fat are found in the chyme. It has been observed by Richet that where the contents of the stomach contain much fat, this appears to be retained in the stomach until all other matters have been expelled.

The Non-Digestion of the Stomach by its own Juice.

The fact that the delicate mucous membrane of the living stomach is not digested by the gastric juice which it secretes, early attracted the attention of observers.

When animals or human beings are killed whilst the digestive process is actively proceeding, it not unfrequently happens that large portions of the stomach are softened and perforated ; the gastric juice then escaping may act upon adjacent organs, partially digesting them, as in a case which came under my notice, in which a part of the spleen had been pretty thoroughly digested, and the left half of the diaphragm had been perforated. The process proceeds most perfectly when the external conditions are such that the body cools slowly ; it affects particularly the fundus of the stomach.

John Hunter attempted to explain the non-solution of the living stomach by the gastric juice as due to its vital properties, which exempted it from an action which dead matter could not resist. But this explanation, besides being open to the objection of a *petitio principii*, is disproved by the fact that living tissues may, under certain circumstances, be digested by the stomach. Thus Claude Bernard found that the legs of a living frog which had been introduced through a fistula into the interior of the stomach of a dog underwent digestion though the animal was alive.

Claude Bernard explained the non-digestion of the gastric mucous membrane as due to its epithelial covering, which is continually being renewed, whilst Schiff believed that the layer of mucus which covers the internal surface of the stomach effectually protects it. The view of Claude Bernard is disproved by the fact that in cases where the continuity of the epithelial covering of the stomach is interrupted, as in gastric ulcer, digestion of the parts deprived of epithelium does not occur. Schiff's view is probably in part true. Scientific opinion has, however, inclined to favour the view of Dr. Pavy, that the non-digestion of the living stomach is connected with the circulation, through the blood-vessels of the mucous membrane, of alkaline blood, whence there is continually transuding alkaline plasma, which bathes the ultimate anatomical elements of the tissues. The acid gastric juice

which could penetrate to these, having its acidity removed, is naturally rendered inert. This view is supported by the fact that when certain of the arteries of the stomach are tied the areas supplied by them are liable to perforation by a process akin to that of *post-mortem* digestion.

LECTURE V.

THE STRUCTURE OF THE DUODENUM—THE BILE AND THE PART WHICH IT PLAYS IN DIGESTION—THE PANCREAS; ITS SITUATION AND STRUCTURE—THE FERMENTS OF THE PANCREAS AND PANCREATIC JUICE.

IN my last lecture I told you that at the beginning of gastric digestion the *pylorus*, or pyloric orifice of the stomach, is tightly closed, but as digestion proceeds it becomes more and more relaxed, so that whilst at first only the finer parts of the gastric contents can pass—in the form of pulpy chyme—afterwards the coarser parts, and even solid lumps of imperfectly digested aliment are permitted to escape into the duodenum.

The chyme when it leaves the stomach possesses a strong acid reaction. On entering the duodenum it encounters, however, the secretions of the glands of the duodenum, but especially the secretions of the liver and of the pancreatic juice, all of which possess an alkaline reaction, so that the acid reaction is soon lost.

Let me direct your attention to the diagrams to which I have before pointed, which exhibit the general arrangement of the organs of digestion (see Fig. 1, p. 39), as well as one (Fig. 19) in which we have the stomach and duodenum laid open, and the point of entrance of the various ducts exhibited.

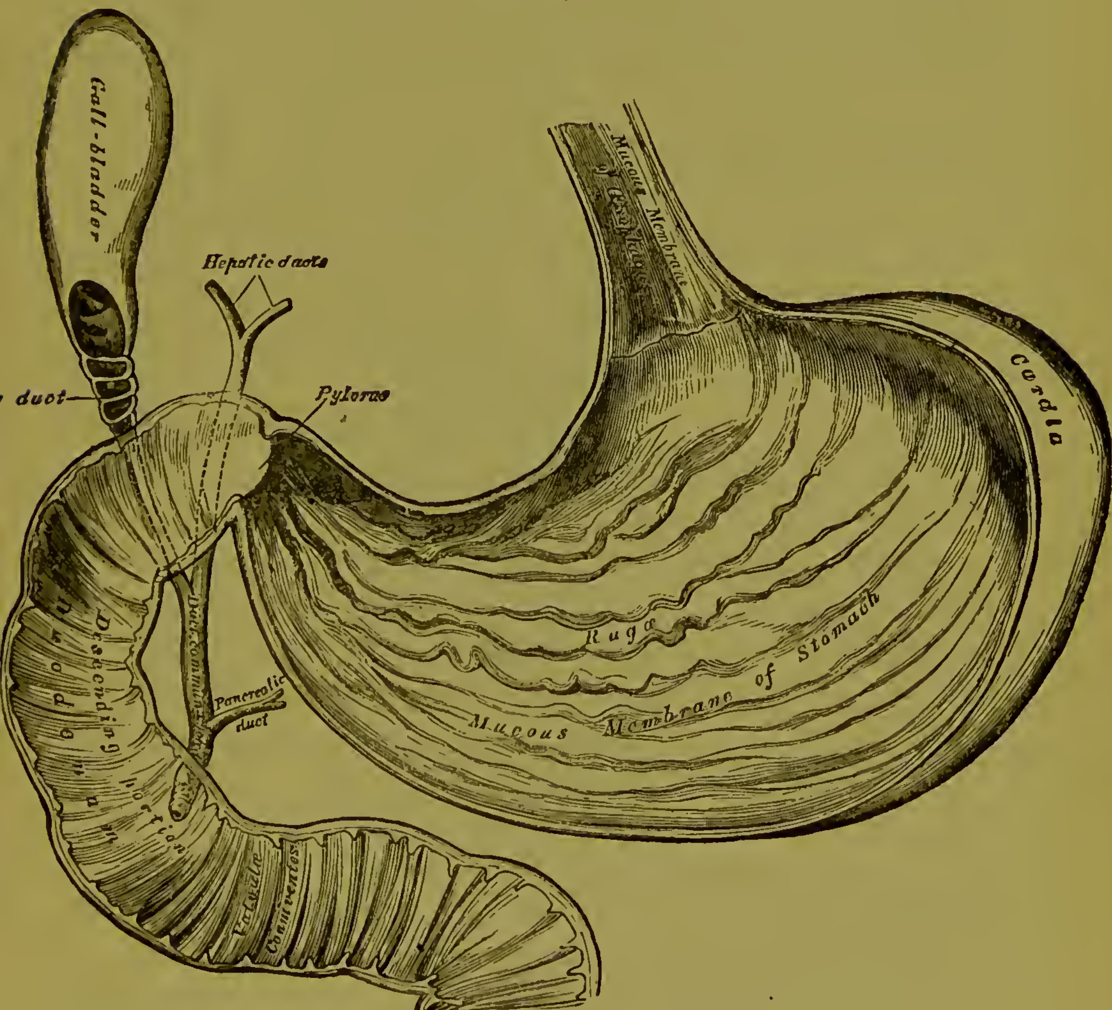
The Structure of the Duodenum.

Before speaking to you of the important chemical operations which are brought about by the digestive juices poured into the duodenum, let me, for a moment only, dwell upon

its structure, which I shall illustrate by a reference to a diagram, which I have had copied from Professor Turner's 'Introduction to Human Anatomy.' (See Fig. 20.)

Observe that the mucous membrane presents the projecting processes or *villi*, which are seen throughout the

FIG. 19.

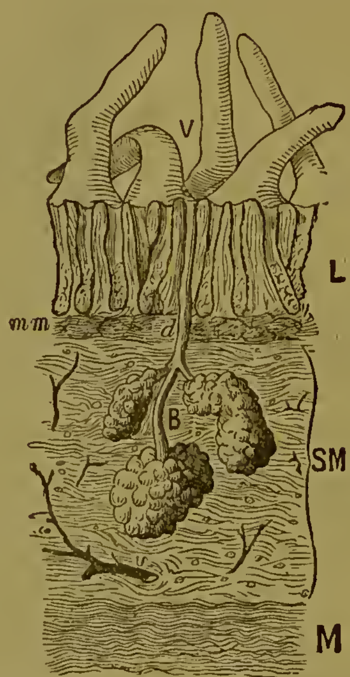


THE INTERIOR OF THE STOMACH AND DUODENUM, WITH THE ENTRANCE INTO THE DUODENUM OF THE COMMON BILE DUCT AND THE PANCREATIC DUCT (GRAY'S ANATOMY).

small intestine, and to whose structure I shall again refer. At the base of these villi, and occupying the greater part of the thickness of the mucous membrane, are placed side by side a number of simple glands, like test tubes, which are

lined by a single layer of columnar epithelial cells. These are the so-called "Glands of Lieberkühn." Glands of precisely similar structure are found in the mucous membrane throughout the course of the small intestine, and essentially the same kinds of glands also occur in the large intestine. The epithelium which lines them unquestionably has for one of its functions the secretion of a liquid containing some mucus, and to which I shall again refer, under the name of

FIG. 20.



VERTICAL SECTION THROUGH THE WALLS OF THE DUODENUM (TURNER).

Showing: V, intestinal villi; L, layer of glands of Lieberkühn; *m*, *m*, tunica muscularis mucosæ; S M, submucous coat; M, a schematic indication of a portion of the muscular coat: B, a gland of Brunner, situated in the submucous coat, with its duct *d*, running between glands of Lieberkühn and opening on the surface of the mucous membrane.

"Intestinal juice." Beneath this layer of glands we observe (Fig. 20, *m m*) imperfectly delineated the layer of involuntary muscular fibres which is called the (tunica) *muscularis mucosae*, and to which I referred, as well as to other matters which I should wish you to remember, in my

second lecture (p. 41). Below this we observe the *sub-mucous* coat.

In this you will notice the lobes of an acinous gland, one of the Glands of Brunner, whose duct opens on the surface of the mucous membrane. The Glands of Brunner are peculiar to the duodenum; they have a structure which, according to Klein, is identical with that of the pyloric glands of the stomach, and they appear, like them, to form a small quantity of pepsin.

To some points in which the duodenum shares more or less the characters of the rest of the small intestines, I shall subsequently direct your attention.

The Bile and its Influence in Digestion.

The Bile is the secretion of the Liver, which is the largest of the glands of the blood. At one time it was believed that the preparation of this fluid was the essential function of the liver. When we take into account the large size of the organ, which in adult human bodies has a weight which amounts to between one twenty-fourth and one-fortieth of that of the body, that its substance contains myriads of protoplasmic masses supplied in a peculiarly lavish manner with blood, we are not surprised to learn that modern research has established that whilst the liver is of all the organs of the body, the one in which chemical changes of the greatest magnitude have their seat, the secretion of bile represents but very imperfectly the activity of the organ.

This great gland secretes daily an amount of bile, which in man, probably amounts to between ten and twenty ounces, though the amount varies, as that of other secretions of the body, with many circumstances, and is particularly influenced by the food of the individual.

The colour of the bile of man and carnivorous animals is, when fresh, reddish brown, and is mainly due to the chief colouring matter termed *Bilirubin.* Its reaction is dis-

tinctly alkaline. The specific gravity of the bile is about 1020, and it probably contains, when freshly secreted, less than two per cent. of solids.

The solid matters of the bile present as their principal components: 1st. The colouring matters, of which the chief is the before-mentioned *Bilirubin.* This has the empirical formula $C_{16} H_{18} N_2 O_3$; it admits of being separated in the form of orange-coloured microscopic crystals, and is undoubtedly derived from the blood colouring matter, oxy-hæmoglobin, of which a certain amount undergoes destruction either in the spleen or liver, or in both of these organs, certain of the products of the decomposition being excreted in the bile. Bilirubin and all the allied bile-colouring matters, as, for instance, *Biliverdin,* which gives the green colour to the bile of herbivorous animals, exhibit the so-called Gmelin's Reaction, i.e., when treated with strong impure nitric acid, a play of colours is produced—green, blue, violet, and red being successively distinguished.

2nd. Sodium salts of the so-called bile-acids, viz., Glykocholic and Taurocholic acids.

The former of these acids has the formula $C_{26} H_{43} NO_6$; and the latter, which contains sulphur, $C_{26} H_{45} NO_7 S$. They are recognized in the bile by the so-called Pettenkofer's reaction, which consists in adding to a little bile on a white plate, a few drops of a watery solution of sugar, and afterwards some strong sulphuric acid, when a beautiful purple colour is produced.

The bile-acids are doubtless products of decomposition of proteid constituents in the liver.

3rd. A beautiful crystalline body termed Cholesterin, $C_{25} H_{42} O$, which is soluble in ether, and was formerly erroneously believed to be a fat. It is an abundant constituent of nerve-fibres, and is found in large quantities in the nerve-centres; whence it is probably removed in part by the blood and excreted by the bile.

4th. The viscid body called Mucin.

5th. Certain mineral salts.

The table to which I point indicates the composition of human bile according to the most recent analyses of Yeo and Herroun.

We have now to consider the uses of the bile in digestion, and these I may dismiss very briefly.

The bile in man and the majority of animals contains no ferment, and therefore exerts no specific action upon any of the organic food constituents. It would be a mistake, however, to believe that it plays no part in digestion. Coming in contact with the acid chyme, as it enters the duodenum, it neutralises in part the free acid which it contains, and so tends to establish one of the conditions necessary to the proper progress of pancreatic digestion. This neutralisation is accompanied by the precipitation in part, at least, of intermediate products of the digestion of proteids, such as hemialbumose, and the precipitate thus occasioned doubtless carries down with it, mechanically, much of the pepsin which exists in the more fluid part of the chyme. It co-operates with the pancreatic juice in emulsionizing the fatty matters of the chyme, whilst it appears to possess the power of influencing the passage of finely divided fats through the mucous membrane. This function of the bile in facilitating the absorption of fats, is one which must not be lost sight of, and which is proved by many facts which I have not the time to bring before you, but which are quite sufficient to disprove the view of those who have spoken of the inutility of the bile in digestion.

Amongst the subsidiary functions of the bile in the alimentary canal, appears that of modifying, in an unknown way, the processes of decomposition which occur in it, for in living creatures, from whose intestinal canal bile is cut off, either by artifice or disease, a peculiarly putrid decomposition of the intestinal contents invariably occurs.

The secretion of the liver is one which, unlike that of the gastric glands or of the prancreas, is continuous, though its activity varies greatly. In man and a large number of animals the secretion is not, however, continually dis-

charged into the duodenum, but may be in part stored in the so-called gall-bladder.

We have seen that the bile possesses some uses in digestion, though it cannot be looked upon as occupying the first rank amongst digestive juices. It is a liquid which, though not without distinct functions, and therefore not to be compared to a simple excretion, such as that of the kidneys, yet is, in the main, an excretion. I am often in the habit of comparing it to the liquid refuse leaving a chemical manufactory, which, by its composition and amount, often conveys but a very imperfect idea of the nature and magnitude of the processes which are carried on in the factory.

To the principal functions of the liver, so far as they are known to us, I shall, in the last of this series of lectures, briefly call your attention.

The Pancreas and the Pancreatic Juice.

The Pancreas is a gland which secretes an alkaline juice, and which empties itself into the upper portion of the small intestine.

It exists in all air-breathing vertebrates—in mammals, birds, reptiles—and in many, though by no means in all, fishes.

Although it has been usual to say that the pancreas does not exist in invertebrates, it would appear from the recent researches of Krukenberg and others that a glandular organ which is the physiological analogue of the pancreas is widely distributed throughout invertebrates.

The Pancreas is a long narrow gland of a yellow cream colour, which during life varies in tint, being pale when inactive, but turgid and roseate in hue whilst secretion is proceeding. In man the organ lies "across the posterior wall of the abdomen, behind the stomach, and opposite the first lumbar vertebra. Its larger end, the *head*, turned to the right, is embraced by the curvature of the duodenum, whilst its left or narrow extremity, the *tail*, reaches to a somewhat higher level, and is in contact with the spleen."

In the figure to which I now point, Fig. 21, you will see the duodenum detached from other parts of the alimentary canal, but with its relations to the gland which is chiefly to occupy our attention, viz., the Pancreas.

Observe running along this elongated gland, a tube, its duct, and follow the dotted lines, which indicate the entrance of the pancreatic duct into the duodenum. You will see that just before reaching the duodenum the pancreatic duct is joined by the so-called "*Ductus communis choledochus*," or common bile duct, which conveys the *bile* from the liver into the duodenum.

FIG. 21.

THE PANCREAS AND ITS RELATIONS TO THE DUODENUM AND SPLEEN. (GRAY'S ANATOMY.)

The normal arrangement is that there exist two pancreatic ducts. One, very much larger than the other, *the* pancreatic duct, properly so-called, or *Duct of Wirsung*,*

* Wirsung was an anatomist of the 17th century who first observed and delineated the pancreatic duct. He is said to have died by the

empties itself into the duodenum between three and four inches below the pylorus by an orifice common to it and to the common bile duct; the second, very small, *accessory* pancreatic duct, communicates with the first by one or more anastomosing branches, and usually has a separate opening into the duodenum. In most animals the chief duct of the pancreas opens into the intestine with, or very near to, the opening of the common bile duct. In some animals, however, as in some monkeys,* in the ox, the guinea-pig, and the rabbit, the principal duct empties itself below the orifice of the bile duct. In the last-named animal the arrangement has been particularly studied by Claude Bernard, who has shown that whilst the accessory duct usually opens by a common orifice with the bile duct, the principal duct empties into the intestines 35 centimeters below that point.†

Minute structure of the Pancreas.

The pancreas used to be described as a compound saccular or racemose gland. The observations of Latschenberger and Heidenhain have drawn attention to the fact, however, that the pancreas is more properly a compound tubular gland, i.e. if we follow its branching ducts we find them terminating in blind tubes, and not in sacculated recesses.

The gland possesses a capsule of connective tissue whence septa proceed inwards, which penetrate the organ and support its constituent lobes and lobules. The interlobular connective tissue supports the blood-vessels, the nerves, and the lymphatics of the gland.

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hands of an assassin in 1643, the same year in which he sent a copy of his engraving of the pancreatic duct to Riolan. (Claude Bernard, 'Leçons de Physiologie Expérimentale,' Vol. II. (1856), p. 171.)

* See Milne Edwards, 'Leçons sur la Physiologie et l'Anatomie Comparée' (1860), Vol. VI. p. 511.

† Claude Bernard, *op. cit.*, pp. 270 and 271.

The pancreas possesses, as has been said, in most animals, two, in some more than two excretory ducts. These ducts are lined by columnar epithelium, which lies upon a basement membrane. On the outer side of this basement membrane there is no inconsiderable amount of fibrillar connective tissue and some involuntary muscular fibres. With the excretory ducts there communicate the lobar ducts, these proceeding outwards lead to intralobular ducts, and these again to so-called *intermediary ducts* which communicate directly with the alveoli.

The epithelium lining lobar and intralobular ducts is composed of short columnar epithelium cells, each with an oval nucleus near the membrana propria on which the cells lie. The epithelium cells become shorter from the lobar towards the *intermediary ducts.* It is to be noted that the epithelial cells of the ducts of the pancreas do not exhibit the "rod-like fibres" (Klein) which are so clearly seen in the intralobular ducts of the salivary glands.

The intermediary ducts "are branched canals of various lengths with a small but distinct lumen; each consists of a membrana propria, a continuation of the same membrane of the intralobular duct, lined with a single layer of flattened clear cells more or less elongated, and each with a flattened oval nucleus" (Klein). In some cases, as in the pancreas of the rabbit, these tubes are very long, in others extremely short, the branches of the intralobular ducts appearing to pass almost into the alveoli.

The alveoli which open into the intermediary canals are more or less tortuous tubes composed of a delicate basement membrane which is covered on its inner side by the proper secreting cells which, as Heidenhain aptly remarks, possess specific peculiarities which make it impossible to mistake them for the cells of any other gland. These cells are sometimes described as columnar, but they are not as regular as typical columnar epithelium cells and present much more rounded outlines. The tube is so filled by these cells that no definite continuous lumen can be made out.

The appearances of the pancreatic cells differ greatly

according as the gland has been for many hours inactive or long secreting. We shall at present only describe the appearance of the cells of the pancreas of the fasting animal.

Each cell presents, in its fresh living condition, a clear *apparently* homogeneous *outer zone*, directed towards the basement membrane, and a granular *inner zone*. The clear outer zone is relatively small, only forming from one-eighth to one-sixth of the depth of the cell. Carmine stains the outer, clear zone easily, but scarcely at all the granular inner zone.

The outer zone which in the living cell appears homogeneous is not so in reality, as we learn by the action of perosmic acid, or by pretty prolonged maceration in solution of neutral ammonium chromate, which reveal the existence of longitudinal fibrillation.

At the junction of the outer and inner zone of the cells of the fasting pancreas is situated a spherical nucleus which is scarcely if at all visible in the living cell, but which is stained by carmine or logwood.

The pancreas in man receives branches from—1st, the hepatic artery; 2nd, the splenic artery; and 3rd, the superior mesenteric artery. The branches from these arteries form numerous anastomoses. A capillary network surrounds the ultimate acini, but by no means closely, so that often the secreting cells are at a considerable distance from the nearest capillaries.

The veins of the pancreas which run by the side of the arteries empty into the superior mesenteric and into the splenic veins, so that all the blood which leaves the organ has to pass through the liver.

General Phenomena of the Pancreatic Secretion.

The general phenomena of the secretion of pancreatic juice have been discovered by observing firstly and chiefly animals in which temporary fistulæ had been established, during the time which elapses before the functions of the

gland become, as a result of the operation, perverted; and, secondly, animals in which permanent fistulæ have been successfully established; as a rule, the fluid obtained from permanent fistulæ soon ceases to be normal.

So long as the condition is perfectly normal the following is the order of events:—

After a fast lasting twenty-four hours or more the pancreas ceases to secrete. Immediately after food has been taken, secretion commences, and the rate of secretion increases rapidly, reaching a maximum some time within the first three hours. The secretion then diminishes until a period which Heidenhain states as extending from the fifth to the seventh hour, when a rise occurs which lasts to the ninth or eleventh hours. The secretion then gradually sinks, until it absolutely ceases; at the seventeenth hour there is then a very scanty secretion; at the twenty-fourth hour all secretion has ceased. The fluid secreted in the early periods of digestion is very viscous, and soon gelatinizes on standing; it is highly coagulable. It contains from 6 to 10 per cent. of solid matters. As digestion progresses, the juice becomes less viscid, its coagulability diminishes, and its solid matters also become less; so that even in the physiological condition we may have a comparatively non-viscid and sparingly coagulable juice.

But in most cases when a pancreatic fistula has been established matters do not continue as above, and the departure from normality is increased, firstly by the secretion becoming continuous; secondly, by its becoming abundant and non-viscous, as well as by another most important character. The normal juice possesses the power, firstly, of digesting proteids; secondly, of converting starch into dextrins and maltose; thirdly, of emulsionising and decomposing the neutral fats. Now the non-viscous, abundant, secretion obtained from the majority of cases of permanent fistulæ only possesses the second and third of these properties; it is, that is to say, destitute of, or at least very poor in, the proteolytic ferment.

Though the close dependence of the secretion of pan-

creatic juice upon the various stages of the digestive process must clearly depend upon nervous control, our knowledge of the nervous mechanism is not as complete as might be wished.

From the analogy to the salivary glands Heidenhain thinks it likely that in the pancreas as in the salivary glands there exists two classes of secretory nerves which influence its activity, viz., truly *secretory*, i.e., which govern the separation of water and salts by the gland, and *trophic*, which by influencing the exchanges of matter in the secreting cells, influence the passage of solid constituents into the secretion.

Bernard pointed out that the fasting pancreas is pale, the active pancreas firm and turgid, and Kühne and Lea have observed the circulatory changes going on in the pancreas of the living rabbit, which are referred to in the subjoined paragraph.

Changes in the appearances of the secretory cells of the Pancreas which accompany secretion. Concomitant vascular changes.

Our knowledge of the remarkable changes which the secretory cells of the pancreas undergo during digestion is derived first of all from the researches of Heidenhain, which have been confirmed by the remarkable observations made by Kühne and Lea, who were able to watch the actual process of pancreatic secretion in the case of the transparent pancreas of young rabbits, which was drawn through a small wound in the abdominal wall, and examined under the microscope, special arrangements being employed which prevented evaporation and cooling. The following is a short summary of the researches of Heidenhain and Kühne and Lea, which I quote from Professor Michael Foster's admirable work on Physiology :—

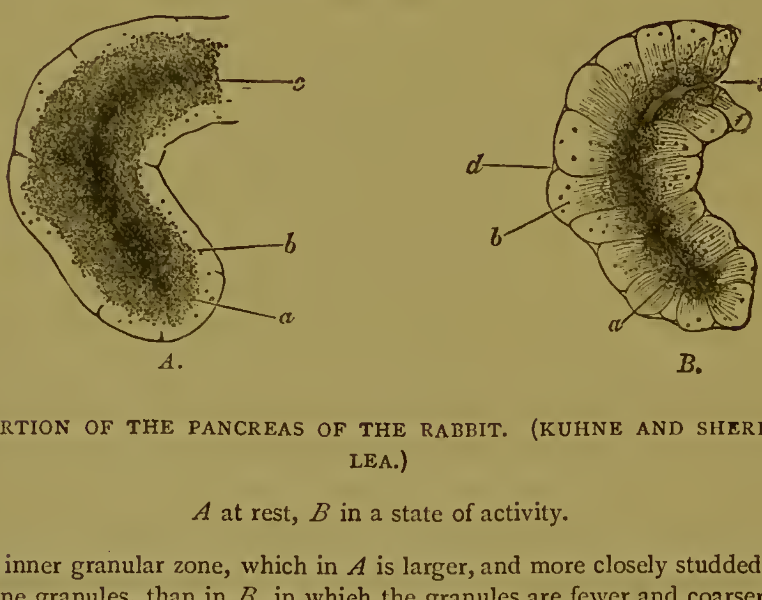
"We learn from the researches of Heidenhain that each secreting cell of a pancreas of an animal (dog) which has been fasting for 30 hours or more consists of two zones : an

inner zone, next to the lumen of the alveolus, which is studded with fine granules, and a smaller outer zone, which is homogeneous or marked with delicate striæ. Carmine stains the outer zone easily, the inner zone with difficulty. The nucleus, more or less irregular in shape, is placed partly in the one and partly in the other zone. When, however, the pancreas of an animal in full digestion (about six hours after food and onwards) is examined, the outer homogeneous zone is found to be much wider, the granular inner zone being correspondingly narrower, and in some cases actually disappearing. The whole cell is smaller, and, owing to the relatively larger size of the outer zones, stains well. The nucleus is spherical and well formed. If the pancreas be examined at the end of digestion, when its activity has once more ceased, and it has entered into a state of rest, the outer zone is again found to be narrow, the granular inner zone occupying the greater part of the cell, which in consequence stains with difficulty; and the whole cell has once more become larger. There seems to be but one interpretation of these facts. During the time that the pancreas is secreting more rapidly, there is a diminution of the inner zone; that is to say, the inner zone furnishes material for the secretion. But while the inner zone is diminishing, the outer zone is increasing, that is to say, the outer zone is being built up again out of materials brought to it from the blood, though not to such an extent as to prevent the whole cell from becoming smaller. When digestion is ended, after the pancreas has ceased to secrete, the inner zone again enlarges, evidently at the expense of the outer zone, though the latter also continues to increase, causing the whole cell to become bigger. From thence till the next meal, there occurs a partial consumption of the inner zone, so that the outer zone becomes more conspicuous again, though the whole cell becomes smaller. Evidently out of the protoplasm of the cell, which is itself formed at the expense of the blood, the granules are formed, and these being deposited towards the lumen of the alveolus distinguish the outer homogeneous from the inner granular zone,

and the secretion is produced at the expense of the granules.

"Kühne and Sheridan Lea,* observing, under the microscope, the pancreas of the living rabbit, have been able to watch the actual process of secretion; and their results, while they extend, in the main corroborate those of Heidenhain. In the quiescent pancreas of the rabbit, Fig. 22 A, the cells are for the most part filled with granules, the transparent outer zone being reduced to small dimensions; the outlines of the individual cells are very indistinct, with the margins of the alveoli smooth; the lumen of the alveolus is obscure; and the blood supply is scanty. Upon secretion being set up, Fig. 22 B, the margins of the active alveoli become indented through a bulging of their constituent cells, the outlines of which now become distinct; the

FIG. 22.



A PORTION OF THE PANCREAS OF THE RABBIT. (KUHNE AND SHERIDAN LEA.)

A at rest, *B* in a state of activity.

a the inner granular zone, which in *A* is larger, and more closely studded with fine granules, than in *B*, in which the granules are fewer and coarser.
b the outer transparent zone, small in *A*, larger in *B*, and in the latter marked with faint striæ.
c the lumen, very obvious in *B*, but indistinct in *A*.
d an indentation at the junction of two cells, seen in *B*, but not occurring in *A*.

* Kühne, 'Ueber das Secret des Pankreas.' *Verhand. d. Naturhist. Med. Vereins zu Heidelberg*, Bd. I. Heft 4.

granules retreat towards the inner zone, bordering on the cavity of the alveolus, and as secretion goes on, evidently diminish in number, the whole cell becoming hyaline and transparent from the border inwards ; at the same time the blood vessels dilate largely, and the stream of blood through the capillaries becomes full and rapid."

In describing the general phenomena of the pancreatic secretion, some of its more prominent physical and chemical characters have been referred to ; we must now examine these more closely.

Before doing so, let me, however, refer to the estimates of the quantity of pancreatic juice secreted in twenty-four hours. Assuming the amount secreted in man to be in proportion to that secreted by the dog, a man would secrete from 211 to 347 grammes (from about $7\frac{1}{2}$ to little more than 12 ounces).

In describing the general phenomena of the pancreatic secretion some of its more prominent physical and chemical characters have been referred to, though a complete description has been reserved for this section.

Physical Characters.

The juice obtained from temporary fistulae or in permanent fistulae when changes in the gland have not occurred, is, as has already been said, a more or less viscid, gluey liquid.

It contains suspended in it constantly certain morphological elements (Kühne). These are :—colourless blood corpuscles of the smaller kind, which exhibit sluggish yet perceptible amoeboid movements ; corpuscles which are larger than the above-mentioned colourless corpuscles, but smaller than the so-called salivary corpuscles of mixed saliva with which, however, they agree in all other particulars. These corpuscles have in their interior granules which exhibit lively Brownian movements and possess one to four nuclei. At favourable temperatures the morphological elements are digested and dissolved.

Claude Bernard described the pancreatic juice as becoming more viscid as it cooled. Kühne has however found that when cooled (as to 0° C.) it undergoes a true coagulation, separating into a gelatinous and a diffluent part. In consequence of this property the pancreatic juice often forms compact opaque clots in silver cannulae.

The pancreatic juice is invariably alkaline; it possesses a saltish taste. The fluid of temporary fistulae has a higher specific gravity than that of even successful permanent fistulae. The former has a specific gravity of 1030, the latter between 1010 and 1011.

General Chemical Characters.

When heated on the water-bath to 75°, pancreatic juice obtained from a temporary fistula coagulates so completely as to become converted into a white opaque mass, from which there separates a slightly opalescent fluid more alkaline than the uncoagulated juice, which is precipitated by acetic acid and contains alkaline albuminate.

When pancreatic juice is dropped into water, the drops coagulate as they fall, the precipitate being soluble in NaCl and dilute acids. When dropped into very dilute acids a similar coagulation takes place, but the coagula are dissolved when shaken up with the acid.

Alcohol added to pancreatic juice produces an abundant white flocculent precipitate which even when washed with, or digested in, absolute alcohol is for the most part soluble in water at 0° C. Acetic acid does not precipitate this watery solution; after being acted upon for some time by acetic acid, a proteid precipitate is obtained on neutralization. The portion of the alcohol precipitate which is insoluble in water resembles a coagulated albumin.

The alcoholic precipitate referred to carries down with it the various ferments whose action will be described in the sequel. The pancreatic juice is precipitated by the concentrated mineral acids, by metallic salts, by tannic acid. Chlorine water added to fresh pancreatic juice occasions a white precipitate. If however this reagent be added to

pancreatic juice which has been exposed to warmth for some time, it occasions a red colour (Tiedemann and Gmelin).

Pancreatic juice undergoes putrefaction with the utmost ease. The red colour above referred to as brought about by chlorine is due to some body yet unknown which results from decomposition. In a juice which exhibits the chlorine reaction decomposition rapidly proceeds a step further, and then the reaction no longer occurs; on, however, adding impure coloured nitric acid to the now foul smelling liquid, a red colour is developed which is due to indol (C^8H^7N).

Normal pancreatic juice contains three distinct ferments, which will be treated of at length in the sequel. These are: 1, a proteolytic ferment which at suitable temperatures and in solutions which are neutral and faintly alkaline, readily decomposes proteids with the production of peptones and amido-acids, such as leucine and tyrosine: 2, a diastatic ferment, similar to that which exists in saliva, converting starches into erythrodextrins, achroodextrins, and maltose: 3, a fat-decomposing ferment which brings about the hydrolytic decomposition of the neutral fats into glycerin and fatty acids. Although these three ferments always co-exist in normal pancreatic juice, in the continuous thin secretion from permanent fistulae, the second and third ferments are sometimes found unaccompanied by the first or proteolytic enzyme.

In 500 c.c. of freshly secreted pancreatic juice obtained from a large number of dogs, Kühne* was unable to discover a trace of tyrosine. Leucine was present, but in so small a quantity as to be only discoverable by the microscope.

The thick flowing secretion obtained from recently established fistulae (dog) contains approximately in 1000 parts,

900	parts of water,	
190	„	organic solid matter,
10	„	inorganic salts.

The organic solid matter is composed mainly of proteids

* Maly, "See Pankreassaft," in Hermann's *Handbuch*, Vol. v. part 1, p. 187. The author does not know the original sources whence these data have been obtained.

and ferments. Generally, the more abundant the flow, the smaller the amount of solid matter in solution. The salts consist mainly (that is to the extent of about seven-tenths) of sodium chloride; the remaining salts are sodium carbonate, with traces of sodium phosphate, earthy phosphates and traces of iron. Thus, in the first of the analyses given in the subjoined tabular view, Schmidt found the inorganic matters per 1000 to be 8·8, and in this the NaCl amounted to 7·35.

The thin juice secreted continuously by permanent fistulae is sometimes not coagulable by heat alone, but requires the addition of an acid. It contains from 10—20 parts per 1000 of solid matters.

COMPOSITION OF PANCREATIC JUICE (C. SCHMIDT).

	I. From temporary fistulae.		II. From permanent fistulae.		
	a	*b*	*a*	*b*	*c*
Water in 1000 parts	900·8	884·4	976·8	979·9	984·6
Solids " "	99·2	115·6	23·2	20·1	15·4
containing					
Organic matters	90·4	—	16·4	12·4	9·2
Inorganic matters	8·8	—	6·8	7·5	6·1

The Pancreatic Ferments considered in Detail.

In discussing the general chemical composition of the pancreatic juice, I have referred to the fact that it possesses very remarkable properties of acting on organic bodies, and that these are supposed to be dependent upon the existence in the juice of three distinct enzymes. I further stated that when the pancreatic juice is precipitated by alcohol, the precipitate which falls carries down with it the ferments. The precipitated body has in past time been supposed indeed to constitute the ferment, and the opinion has also been expressed that this ferment is possessed of various properties. We now know, however, that the cause of the activity

of the so-called *pancreatin* is a mechanical entanglement of three ferments, which apparently are not associated with one body but are distinct bodies.

We must now in the first place carefully examine the chief facts relating to each of the ferment actions of the pancreatic juice, and study the products which take their rise in these.

Preparation of active Solutions containing the Ferment of the Pancreas.

It is exceedingly convenient to have at our disposal permanent solutions of the ferments of the pancreas.

1. All the pancreatic enzymes are extracted by glycerine from the gland, and such glycerine solutions may be conveniently preserved.

2. They are likewise soluble in a saturated aqueous solution of chloroform, and the solution keeps very well (Roberts). The presence of chloroform interferes, however with the operation of testing for sugar by Fehling's solution.

3. Roberts has found that for experimental purposes a good and lasting extract of the pancreas may be made by extracting the organ with a solution which contains "three or four per cent. of a mixture of two parts of boracic acid and one part of borax."

4. One of the best methods of preparing a very active solution of the pancreatic enzymes is the following (Roberts) in which advantage is taken of the fact that they are very soluble in water and that their aqueous solutions are preserved from decomposition by a small addition of alcohol :—

Digest fresh pancreas freed from fat and chopped up in four times its weight of dilute alcohol, containing 25 per cent. of rectified spirit (*i.e.* of alcohol of sp. gr. 0·838). The digestion is continued for four or five days with occasional agitation. The mixture is then filtered through paper. Filtration is much facilitated by the addition to the solution of 0·02 per cent. of acetic acid (containing 28 per cent. of the anhydrous acid).

5. The so-called "*pancreas-powder*" of Kühne is an admirable preparation from which solutions of the proteolytic ferments of the pancreas can be prepared at any time. It is made as follows:—Pancreas of the ox is completely extracted with alcohol and ether. There is left a white, friable, dry mass. One part by weight of this solid is digested in the incubator for four hours, with from five to ten parts by weight of a solution containing 0·1 per cent. of salicylic acid; the solution filtered from the insoluble matter is extraordinarily rich in *trypsin*.

1. *The Diastatic Ferment.*

The saliva, we have seen, is a liquid which only possesses an amylolytic action in a few animals, and the great majority of animals have a saliva which possesses no diastatic ferment.

Valentin is said to have first discovered that the pancreatic juice possessed diastatic properties; the fact was apparently independently discovered by Bouchardat and Sandras who obtained the pancreatic juice of hens and geese.

The action of pancreatic juice on raw starch is but slight, on starch mucilage it is surprisingly great. At 35° the action is so energetic that, according to Kühne, it does not admit of being estimated. The diastatic action of the diffluent, abnormal, secretion from permanent fistulae is said (Kühne) to be as powerful as that of the coherent concentrated liquid of permanent fistulae.

An infusion of the pancreas acts upon starch exactly as the pancreatic juice, and we may therefore in our experiments on the diastatic enzyme of the pancreas employ such an infusion instead of the hardly to be procured pancreatic juice.

The action of the diastatic ferment of the pancreas and pancreatic juice appears to resemble in essential particulars that of the saliva and salivary glands; *i.e.*, the products formed are the same, the conditions of activity

are similar, &c. According to Musculus and v. Mehring in both cases there are formed achroodextrins, maltose, and a little grape-sugar.

Roberts has found that the action of pancreatic diastase on starch mucilage increases in speed from zero to 30° C. From this to 45° C. the rate of action continues steady. Above 45° the action becomes slower and slower and ceases between 60° and 70°.

We have seen that within a certain range of temperature, the rapidity of the action upon starch increases. Temperature and all other conditions being exactly similar, the rapidity of the action will depend upon the quantity of enzyme present. This is well brought out in the following remarks (Roberts).

"The speed at which a given quantity of starch is transformed by diastase depends essentially on the proportion of ferment brought to act upon it. In the above experiments (experiments in which a minimal quantity of diastatic solution acted upon starch) the proportion of diastase was very minute in comparison with the amount of starch, and the action went on slowly for forty-eight hours. But if we reverse these proportions and mix a small amount of starch with a large amount of diastase the transformation is instantaneously accomplished. If a test-tube be half filled with an active extract of pancreas and a few drops of starch mucilage be quickly shaken therewith, you cannot detect the reaction of starch or dextrine in the mixture, however prompt you may be with the testing—the transformation has followed on the admixture as instantaneously as the explosion of the charge follows the fall of the trigger. Between these extremes there are all gradations."

Roberts has estimated that pancreatic diastase "is able to transform into sugar and dextrin no less than 40,000 times its own weight of starch.

Had I sufficient time at my disposal I should enter at length into the question as to whether the diastatic ferment of the pancreas exists preformed in the cells of the gland, or whether these contain an antecedent or so-called *zymogen*

of the diastatic ferment, analogous to the zymogen of the proteolytic ferment, to be afterwards briefly referred to.

I may, however, in passing, say that the researches of Liversidge carried out many years ago in Foster's laboratory, leave no doubt as to the existence of such a zymogen of the diastatic ferment.

Want of time prevents, likewise, my examining with you the evidence which leads me to assert that without doubt the several ferment actions of the pancreas depend upon distinct ferments, and are not different attributes of one body.

2. *The Fat-decomposing Ferment.*

It was in the year 1846 that Claude Bernard, being engaged in a comparative study of the process of digestion in carnivorous and herbivorous animals, was struck by the fact that when dogs were fed upon fatty matter this appeared to undergo a modification almost as soon as it passed into the small intestine, whilst when rabbits were similarly fed the change occurred somewhat further from the pylorus. Again, Bernard observed that after a fatty diet the lacteals of dogs were filled with white opalescent chyle from the pylorus downwards, whilst in rabbits the lacteals near the pylorus did not contain white chyle, while those situated lower down did. Bernard then discovered that this difference in the appearance and absorption of fatty matters coincided with the difference in the situation at which the pancreatic duct joins the small intestine in the dog and rabbit respectively. In the dog the principal duct empties itself, together with the bile duct, into the duodenum very near to the pylorus ; whilst in the rabbit the principal duct joins the small intestine from 30 to 35 centimetres (12 to 14 inches) below the point of entrance of the bile duct.

When this relationship had been found to exist between the situation at which the pancreatic juice is poured into the intestine and the situation where fat begins to be modified, it was natural to inquire whether the juice was not the active agent in effecting the modification of fatty

matter, and in causing the appearance of milky chyle in the lacteals, and as the result of his investigations Claude Bernard was led to the discovery of the facts about to be commented upon.

Oil or fatty matters which are fluid at the temperature of the animal body are very readily emulsionised by the pancreatic juice.

If two parts of alkaline and viscous pancreatic juice, be shaken up in a test-tube with one part of olive oil, a perfect emulsion is almost instantly obtained, the liquid resembling milk or chyle; the same result is obtained if we substitute for olive oil fats, such as butter or mutton suet, which melt at a temperature below 40° C. Temperature appears to have considerable influence in the process. Thus, when one gramme of lard is agitated with two grammes of fresh, normal, pancreatic juice, the process of emulsionising commences even in the cold, but when the temperature is raised to 35° or 38°, a white creamy emulsion is obtained instantly. Emulsions obtained in this way are remarkably persistent, and, according to Kühne, the fat in them exists in even a finer state of division than in milk.

The so-called Pancreatic Emulsion of Messrs. Savory and Moore, which for many years has been used in medicine, is a preparation in which this power of the pancreas of bringing about the emulsionising of fats has been taken advantage of, so as to obtain fats in an extremely fine state of division, in which condition they appear to be most readily absorbed from the alimentary canal.

Claude Bernard was led to believe that the property of emulsionising fats which the pancreatic juice possesses in so extraordinary a degree, depended upon a ferment, which at the same time occasioned the remarkable change to be immediately referred to, and which he termed the '*Emulsive Ferment.*' In this view Bernard was probably wrong. It is probably only in an indirect way that a ferment leads to the emulsionising of the fats.

Brücke has shown that when an oil or a fat which contains a mere trace of free acid, is shaken with a weak solution of

carbonate of soda, an emulsion is readily obtained, whilst if the oil be perfectly neutral no such emulsion is obtained. It will be shown that at the temperature of the body the pancreatic juice does lead to the acidification of fats ; as the juice does contain carbonate of soda, the conditions arise readily which are required for the production of an emulsion. It is remarked by Kühne, and with justice, that probably the proteid matters in the pancreatic juice play an important part in the emulsionising action.

Bernard discovered that when emulsions are made by mixing fresh, alkaline pancreatic juice with a neutral fat, such as olive oil or lard, and the emulsions are maintained at the temperature of the animal body, an acid reaction is very soon developed. The observation has been confirmed again and again, by Berthelot amongst others.

Claude Bernard had found that when butter is kept at the temperature of the body with pancreatic juice, the odour of butyric acid is soon perceived.

Berthelot tried the experiment with synthetically prepared monobutyrin, and found that by the action of pancreatic juice upon it there was obtained besides undecomposed monobutyrin, a mixture of free glycerin, butyric acid and a soap.

The property which the pancreatic juice possesses of decomposing the neutral fats is shared by the pancreatic tissue itself ; it is indeed laid down by Claude Bernard as the characteristic of this tissue that it possesses the property of *instantaneously* decomposing butyrin.

This property is, however, only possessed by the perfectly fresh tissue of the pancreas, and by extracts made with peculiar care. It is, however, unquestionably possible to obtain clear glycerin-extracts of pancreas endowed with powerful fat-decomposing properties.

Grützner has found that the richness of the pancreas in the fat-ferment varies, and in the same sense as its richness in diastatic and proteolytic enzymes. Thus the pancreas of a dog is poorest in the fat-ferment about six hours after a rich meal. Thereafter the amount increases up to the

fortieth hour, so that the pancreas of fasting animals is richest in the fat ferment.

Grützner believes that the central zones of the pancreatic cells not only form the proteolytic, but likewise the fat-decomposing and diastatic ferments.

The action exerted by the fat-decomposing ferment is one in which the fat combines with the elements of water; an example of what is often termed a hydrolytic decomposition. The following is the reaction which occurs under the influence of the ferment when stearin is decomposed.

$$\underbrace{C_{57}H_{110}O_6}_{\text{Tristearin.}} + 3\ \underbrace{H_2O}_{\text{Water.}} = \underbrace{C_3H_8O_3}_{\text{Glycerin.}} + 3\ \underbrace{C_{18}H_{36}O_2}_{\text{Stearic Acid.}}$$

3. *The Proteolytic Enzyme of the Pancreas—Trypsin.*

Corvisart first discovered that pancreatic juice possesses in a very high degree the property of digesting proteids, and that, indeed, weight for weight, it possesses a much more intense proteolytic activity than the gastric juice.

Strongly opposed by Claude Bernard, the experimental results of Corvisart did not attract the attention which they deserved, and it was not until a now famous research of Professor Kühne, that serious attention was again paid to the proteolytic action of the pancreas.

Kühne pointed out that if the finely divided pancreas of a dog in active digestion be made to act upon well boiled blood fibrin, suspended in water, preferably with the addition of a small quantity of sodium carbonate or hydrate, the fibrin is dissolved in large quantities.

The solution is found to contain besides certain intermediate products of digestion, large quantities of peptones, and considerable quantities of leucine and tyrosine, two bases to which reference will again be made. Usually, unless special precautions are taken, the products of digestion assume an intensely foul odour, due chiefly to the presence of indol and skatol.

The first researches of Kühne have been in the fullest degree confirmed and much extended.

From these it results that the pancreatic juice contains a ferment to which he has given the name of *Trypsin*, which possesses, like Pepsin, strong proteolytic powers. Unlike pepsin, trypsin is absolutely inactive in a strongly acid solution, and indeed at a favourable temperature, trypsin is digested and destroyed by pepsin and hydrochloric acid, and even by the latter alone. Trypsin acts most favourably when present in an alkaline solution, as for instance in a solution containing from one to two per cent. of sodium carbonate, or sodium hydrate. It is to be noted, however, that whilst pepsin is only active in a solution containing *free acid*, *trypsin* can digest in a *feebly acid*, *neutral* or *alkaline* solution, the latter being however much the most favourable.

Long heating, even at moderate temperatures, however, soon destroys the activity of an acid solution of trypsin, just as long digestion of an alkaline solution of pepsin destroys the ferment.

Whilst the production of peptones and amido-acids is rapidly brought about under favourable conditions of temperature and alkalinity, by trypsin alone, the putrid decomposition which has been already referred to as frequently supervening in the course of pancreatic digestion, has nothing whatever to do with trypsin, but is connected with the development of bacteria.

I shall not trouble you with a description of the highly complex processes whereby Kühne has attempted to isolate trypsin—processes which have led to the separation of a body which is a proteid, and which possesses in an intense degree the power of pancreas extracts, to dissolve proteid bodies. It may be, that the ferment in the purest form in which it has been obtained is in reality a mixture of an albuminous substance and a non-proteid ferment. This view, which is supported by the analogy of pepsin, is, however, by no means more probable than that which considers trypsin as containing a proteid body endowed with marvellous ferment actions, for I would point out that the pancreatic juice differs from any other secretion of the body in the fact that it is, normally, intensely coagulable.

I have already referred to the discovery which Heidenhain made that the pancreas does not contain when at rest ready-formed trypsin, but an antecedent or precursor of the ferment, to which he gave the distinctive name of Zymoyen, *i.e.* a body which under various circumstances, when contained in the gland or in extracts of it, may yield the ferment. The accuracy of the fact has received full confirmation, and in the case of other ferments (*pepsin* and the *rennet ferment*), antecedents have been found, which we must call their special zymogens, so that we are compelled to define the special ferment antecedent which we are now considering "*Trypsin-zymogen.*"

Recalling what we have already said of the characteristics of the secreting cells of the pancreas, you will remember that whilst they differ but little microscopically from those of such a salivary gland as the parotid, they exhibit very marked differences, corresponding to their different states of functional activity. During a period of glandular repose the cells appear large, and contain innumerable granules, which are congregated at that side of the cell which lies towards the centre of the acini. The outer or peripheral portion of the cells—the smaller part of the resting cell—is clear. After a period of glandular activity the granular half of each cell is found to have diminished greatly; the whole cell is clear and distinctly smaller than before, and its behaviour towards colouring matters is very different. The pancreas, when perfectly fresh and just removed from the yet warm body of an animal which is killed, does not contain, ready formed, all the ferments which will in the sequel be referred to as characterizing the pancreatic juice. If we treat the gland, for instance, with glycerin, which possesses the power of extracting and dissolving all the ferments, we fail to obtain a solution which possesses the power of digesting proteids; but, instead, we find in the solution a substance from which, by the addition of a little acetic acid, the proteolytic ferment may be formed. The cells of the pancreas thus elaborate a substance which is

the antecedent of the proteolytic ferment, and which yields it when it passes into the pancreatic ducts.

The secretion of pancreatic fluid is slight except during digestion. After the taking of a full meal the secretion is suddenly exalted, reaching its maximum two or three hours afterwards. The secretion then diminishes until a period which extends from the fifth to the seventh hours, when a rise occurs, which lasts to between the ninth and eleventh hours after food. The secretion then gradually sinks, until it absolutely ceases.

Stimulation of the gastric mucous membrane starts the secretion of pancreatic juice ; it is arrested during nausea and vomiting, as also when the central end of the divided pneumogastric is stimulated.

In my last lecture I shall examine with you more carefully than I have yet done the products of the pancreatic digestion of proteids, and touching briefly upon the other changes which have their seat in the alimentary canal, conclude this brief sketch of the Function of Digestion by a reference to the channels by which the products of digestion are conveyed to the blood, and by an outline of certain of the chemical processes of nutrition.

LECTURE VI.

THE PRODUCTS OF THE PANCREATIC DIGESTION OF PROTEIDS — INTESTINAL JUICE — ACTION OF FORMED FERMENTS IN SMALL AND LARGE INTESTINES—ABSORPTION OF THE PRODUCTS OF DIGESTION.

IN my last lecture, besides giving you a general sketch of the action of the pancreatic juice on proteids, I pointed out with some care the main differences between trypsin and pepsin. I now wish to treat, though in a very elementary manner, of the nature of the changes brought about in proteids by these two ferments.

The various ferments of the alimentary canal all resemble in this,—that the changes they bring about are decompositions of complex into simpler bodies, the complex bodies combining with the elements of water before decomposition—decompositions which, since Hermann introduced the expression, have been termed "Hydrolytic." Thus we saw that the results of the diastatic action of saliva upon starch might be represented by the equation—

$$\underbrace{10(C_{12}H_{20}O_{10})}_{\text{Starch.}} + \underbrace{8(H_2O)}_{\text{Water.}} = \underbrace{(C_{12}H_{20}O_{10})_2}_{\text{Achroo-dextrin.}} + \underbrace{8(C_{12}H_{20}O_{11})}_{\text{Maltose.}}$$

And that the action of the fat decomposing ferment of the pancreas upon stearin might be represented by the equation—

$$\underbrace{C_{57}H_{110}O_6}_{\text{Tristearin}} + \underbrace{3H_2O}_{\text{Water}} = \underbrace{C_3H_8O_3}_{\text{Glycerin.}} + \underbrace{3(C_{18}H_{36}O_2)}_{\text{Stearic Acid.}}$$

In these cases we have complex molecules combining with the elements of water and breaking up into much more simple molecules.

The decompositions brought about by these ferments are very similar; in the second case referred to, indeed, abso-

lutely identical with those which are occasioned by the action of superheated steam, or by the long continued action of mineral acids of greater or less strength.

In the case of starch, the action of dilute mineral acids is to break up the complex molecule into simpler isomeric molecules, various dextrins, the ultimate product being a sugar: not, it is true, identical with that chiefly produced by diastatic ferments, viz. maltose, but readily obtained from the latter, viz. grape sugar.

The products of the action of the proteolytic ferments of the alimentary canal, similarly, presents great resemblance to the substances obtained from proteids by the action of superheated steam, or by long boiling with more or less diluted mineral acids, though, as might be expected, minor differences result from the difference in the conditions.

Essentially, however, it may be stated that the processes are similar in the various cases, and that, under the influence of pepsin and trypsin, the proteid molecule, which is of very high complexity, is resolved into bodies of simpler molecular weight and of less complexity.

The subject which is engaging our attention is one of great difficulty and of remarkable complexity, and I can only pretend to give you, somewhat dogmatically, an outline of the views which have been advanced on this matter by the eminent scientific man who has chiefly investigated it.

Kühne several years ago advanced the idea that when the proteid molecule is digested by means of pepsin and dilute hydrochloric acid, the complex molecule is decomposed (probably hydrolytically) into simpler bodies, belonging to two groups—a *hemi*-group and an *anti*-group, the ultimate products being *peptones;* those derived from the hemi-group being hemi-peptones, and those derived from the anti-group being anti-peptones.

Though possessed of essentially the same reactions, the great and characteristic difference between the two kinds of peptones being, according to Kühne, that anti-peptones are remarkably stable, whilst hemi-peptones, under favourable conditions, as for instance under the influence of trypsin in

presence of an alkali, are decomposed, with the production of other bodies, amongst which are most conspicuous—

Leucine ($C_6H_{13}NO_2$) and Tyrosine ($C_9H_{11}NO_3$)

The following represents the scheme of the proteolytic digestion of proteids by Pepsin, according to Kühne :—

Albumin + Pepsin + Dil. HCl.

Anti-Albumose. Hemi-Albumose.

Anti-peptone. Anti-peptone. Hemi-peptone. Hemi-peptone.

Many looked upon the very briefly and somewhat dogmatically expressed views of Kühne as purely hypothetical, though their probability was enhanced by the studies of Schützenberger who, following other methods of decomposing proteids, had discovered similar facts and arrived at similar conceptions. The further researches of Kühne carried out in conjunction with Chittenden have, however, singularly confirmed his views, and have demonstrated the actual existence of several definite products of digestion whose existence had been previously little more than surmised.

Hemi-albumose is perhaps the best studied of the intermediate products of the digestion of proteids. It is a body which was described by Meissner as A—Peptone ; it is, like the true peptones, highly soluble in water and gives the characteristic ' peptone ' rose reaction, to which I previously referred, when treated with cupric sulphate and sodium hydrate. It is, however, distinguished from peptones by the following reactions.

1st. It is precipitated from its solutions by acetic acid and solution of potassium ferrocyanide ; unlike the precipitate produced under these circumstances by proteids in general, that yielded by hemi-albumose disappears on heating and reappears on cooling.

2nd. It is precipitated from its solutions when these are heated, and reappears on cooling.

3rd. It is precipitated by dilute nitric acid, the precipitate dissolving when the solution is heated and reappearing when it is cooled.

4th. It is precipitated when its solutions are acidified with acetic acid and strong solution of sodium sulphate and boiled.

5th. It is precipitated by metaphosphoric acid.

Hemi-Albumose can be obtained by interrupting peptic-digestion and neutralizing the solution. The precipitate contains anti- and hemi-albumose. The latter is separated in virtue of a property which it possesses of being soluble in five per cent. solutions of sodium chloride.

Apart from the *conditions* favourable to the digestion of proteids by pepsin and trypsin, the essential difference is that pepsin can only split up proteids to a certain extent—reducing them to the state of peptones—whilst trypsin can act upon one group of these and further split them up.

The scheme of trypsin digestion is as follows :—

Proteid + Trypsin.

Anti-Albumose. Hemi-Albumose.

Anti-peptone. Anti-peptone. Hemi-peptone. Hemi-peptone.

Leucine. Tyrosine. Leucine. Tyrosine.
&c. &c. &c. &c.

I would direct your attention very particularly to the fact that whilst Leucine and Tyrosine are the most characteristic and readily identified of the further decomposition products of the hemi-peptones, there are unquestionably others.

With reference to Leucine and Tyrosine I would add the following remarks. The former body, which has the empirical formula $C_6H_{13}NO_2$ may be represented as

$$\begin{array}{l} C_5H_{10}\text{—}NH_2 \\ | \\ COOH \end{array}$$

and is amido-caproic acid.

Tyrosine, on the other hand, is a more complex body, which we may regard as Parahydroxylphenyl-alpha-amido-propionic acid.

$$C_6H_4\begin{cases} OH \\ C_2H_2\begin{cases} NH_2 \\ COOH \end{cases} \end{cases}$$

Before leaving the products of artificial pancreatic digestions, I must mention that on the addition of a weak solution of bromine in water to a liquid in which pancreatic digestion is already proceeding, a violet colour is developed.

Having studied the products which are obtained when proteids are artificially digested with the proteolytic ferment of the pancreas, we naturally ask ourselves the question: how far do the processes which go on in the alimentary canal resemble those which occur *in vitro?* To this question

I shall give an answer in a general survey of the digestive processes of the small intestines.

The Intestinal Juice.

By the name of intestinal juice, or *Succus Entericus*, we designate the liquid which is secreted by the glands of Lieberkühn, which, as I have told you, are found in the mucous membrane throughout the whole small intestines. Very little is known as to the properties of this fluid. According to the most known accounts, it is an alkaline fluid of specific gravity of 1011, and containing about 2·5 per cent. of solid constituents. It appears to possess very little, if any, proteolytic power, but has a slight diastatic action, and is said to contain an inverting ferment, *i.e.* a hydrolytic ferment which decomposes cane sugar into grape sugar and an isomeric sugar called levulose, thus—

$$\underbrace{C_{12}H_{22}O_{11}}_{\text{Cane Sugar.}} + \underbrace{H_2O}_{\text{Water.}} = \underbrace{C_6H_{12}O_6}_{\text{Levulose.}} + \underbrace{C_6H_{12}O_6}_{\text{Dextrose or Grape Sugar.}}$$

A Survey of the whole Digestive Processes in the Intestines.

We are now in a position to combine the information which we have obtained, and to give a brief summary of the processes which go on in the small and large intestines.

I told you that after sojourning in the stomach for a considerable time the chyme containing both soluble constituents which had escaped absorption in the stomach and yet unacted upon insoluble constituents, passed the pyloric valve and entered the duodenum. Coming in contact with the bile and pancreatic juice, pepsin digestion comes to an end and trypsin digestion commences ; the proteids which have escaped the action of gastric juice succumb to the action of trypsin. The digestion of starches which had been arrested by the acidity of the stomach recommences under the influence of the diastatic ferment of the pancreas, whilst the fats, under the influence both of the bile and the pancreatic juice, are rapidly emulsified.

To what extent, it will be asked, does the digestion of proteids proceed under the influence of the pancreatic juice? Are all the insoluble proteids dissolved, and, if so, do the hemi-peptones as in the beakers in our laboratory, fall to pieces in the intestines, and yield us leucine, tyrosine, asparagine, glycocoll, and other bodies?

To these questions I would answer, that unless under very exceptional circumstances, the proteids which have passed the pyloric valve are completely dissolved, and rendered fit for absorption, so that the fæces of animals fed upon a very large excess of meat do not contain proteids, unless the excess in diet has led to morbid conditions. Whether the hemi-peptones undergo to any considerable extent decomposition, into leucine and tyrosine, is however very problematical. In all probability the peptones are absorbed almost as soon as they are produced, and find their way into the blood, and I hold it to be exceedingly unlikely that in health any but traces of leucine and tyrosine are absorbed.

The various processes which I have referred to are greatly aided by the movements of the intestinal canal, and are associated with the processes of absorption to be afterwards briefly glanced at.

If we except the inverting action exerted by the intestinal juice, it is probable that this fluid plays little but a mechanical part in intestinal digestion.

As the contents of the intestine are followed from above downwards, they are observed to undergo a great diminution in amount, owing to the absorption of water holding the diffusible products of digestion in solution. As the contents pass from the small into the large intestine the reaction which had been alkaline becomes acid, and products of putrefactive decomposition make their appearance.

In this part of the alimentary canal the action of unformed ferments ceases, and the changes which occur are due to *organized ferments*. In some animals, as in the herbivora, the influence of these is probably of the greatest importance, breaking up such constituents as cellulose,

which, as my own experiments long ago showed me, is unacted upon by any of the unorganized ferments of the alimentary canal.

The Intestinal Movements. The Fæces.

When the gastric contents, to which the term chyme is often applied, pass through the pylorus into the duodenum, they begin to move onward by the peristaltic action of the small intestines. The powerful annular fibres contract one after another, driving the food onward, as water may be squeezed along an india-rubber tube by the compression of the hand. The longitudinal fibres contract in such a manner that the intestine is drawn over the advancing mass. The movements always occur (in health at least) in a direction from the stomach to the ileo-cæcal valve; here they stop and never pass as a continuous wave to the large intestine.

Peristalsis may be exhibited by an excised intestine independently of any extrinsic nervous apparatus. Stimulation of the vagus nerve, as a rule, excites the intestinal movements, while excitation of the splanchnic nerves tends to still them. When the blood stagnates in the intestinal vessels active peristalsis ensues. As the splanchnic nerves are also the vaso-motor nerves of the intestines, their excitation produces constriction of the blood-vessels and comparative bloodlessness.

After passing through the ileo-cæcal valve the intestinal contents, which have been very greatly diminished in amount owing to the process of absorption which has gone on quickly, assume the characteristic appearance of fæces. The undigested and insoluble parts of the food, mixed with mucus, with epithelial débris, and with some substances derived from the secretions of the alimentary canal, notably with some biliary products, must be cast out; this is effected by the act of defæcation. The anus is normally kept firmly closed by the contraction of two sphincter muscles,—the external, which is one of the skeletal muscles, and the

internal, which is formed by a special development of the lowest rings of the circular layer of muscles of the intestine. In the act of defæcation these sphincters are relaxed, while the contraction of the rectum forces its contents downwards. The levatores ani are brought into play by the will and exert an action similar to that previously referred to as performed by the longitudinal fibres of the intestine. Of special influence in aiding the expulsion of the contents of the bowel is the contraction of the abdominal muscles which follows a preliminary fixation of the diaphragm by a deep inspiration.

The act of defæcation is essentially a reflex act. The centre, which presides over the sphincters of the anus, lies in the lumbar portion of the spinal cord. This centre is under the control of the brain, under the influence of which its activity is either increased or inhibited.

Absorption of the Products of Digestion.

Absorption of material from the alimentary canal takes place, in part, directly by its passage into the blood-capillaries, and, in part, indirectly, by its passage into the lymphatics, which are exceedingly abundant in the mucous membrane of the stomach and intestines.

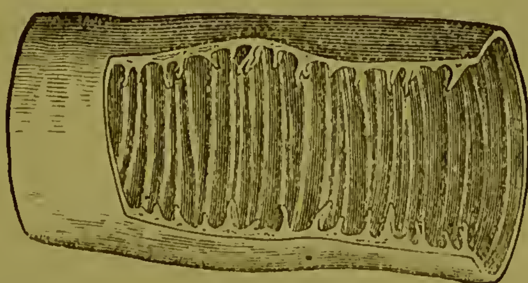
Water, soluble salts, dextrins (?), sugars, peptones, perhaps some of the intermediary products of proteid digestion, such as hemi-albumose as well as emulsioned fats, are the materials present in the alimentary canal which are taken up by the blood-vessels and lymphatics.

That absorption of water occurs in the stomach with remarkable rapidity is proved by the instant alleviation of thirst when water is drunk—an alleviation which of necessity implies the passage of water into the blood; the quick absorption of some highly diffusible bodies is similarly proved by the very rapid excretion of some salts, as, for instance, of potassium iodide, by the salivary glands and by the kidneys, when these salts have been swallowed. In the stomach, doubtless, water and the more highly diffusible

constituents, are rapidly absorbed, and in all probability to a greater extent by the capillaries than by the lymphatics. We cannot suppose, however, that the exceedingly abundant lymphatics of the mucous membrane have no important absorbent functions, though we cannot positively assert what precise share of the work of absorption falls to them.

It is in the small intestine, doubtless, that absorption of the dissolved organic solids of our food chiefly occurs. The large surface of the mucous membrane of this part of the alimentary canal, with its innumerable villi, offers an absorbing surface of large extent pervaded by meshworks of capillaries, and by the commencement of the lymphatics " the *lacteals*." In considering the extent of this surface, let me here particularly draw your attention to the peculiar arrangement of *valvulae conniventes* which I referred to in my second lecture. These so-called valves are crescentic folds of the mucous membrane, which is doubtless arranged in this manner to afford in a given area a larger amount of absorbing surface than would otherwise be possible.

FIG. 23.



SECTION OF INTESTINE WITH A PORTION OF THE WALL REMOVED TO EXHIBIT THE VALVULAE CONNIVENTES (QUAIN'S ANATOMY).

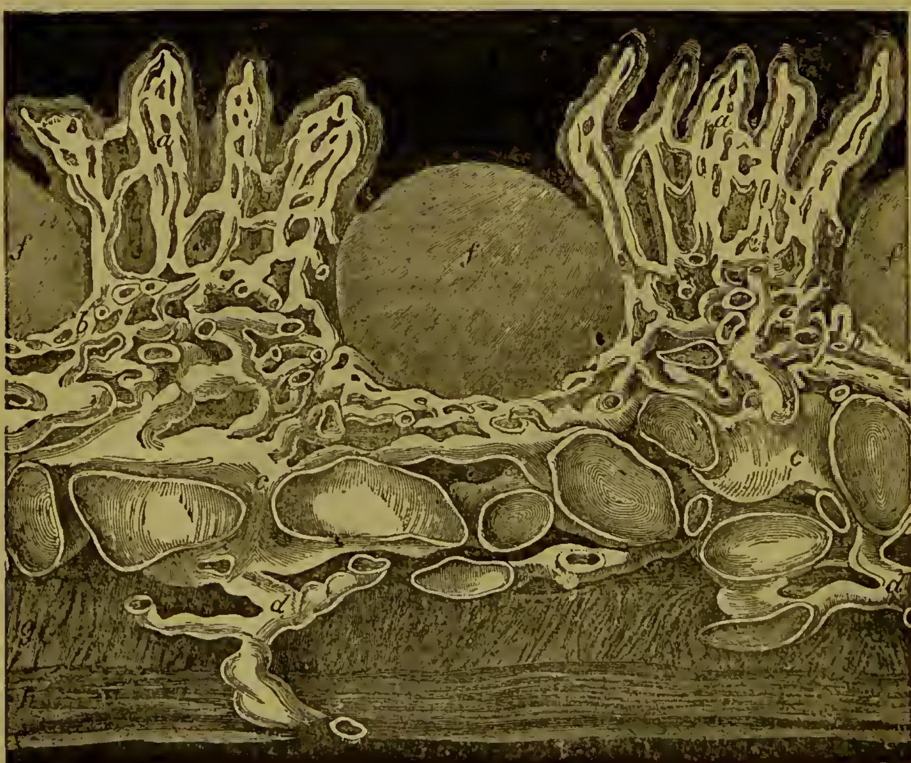
The peristaltic movements of the intestines as a whole, the slighter movements of the mucous membrane and its folds, through the action of the Tunica Muscularis Mucosae, lead to a mixing and progressive movement of the intestinal contents most favourable to absorption.

Before examining particularly the part played by those most important structures *the villi*, in the absorption of nutritive matters from the small intestine, let me refer to

what I said concerning them and the lymphatics of the alimentary canal, in my second lecture, drawing your special attention to diagrams which will illustrate the points of greatest physiological import.

" A further enlargement is effected in the small intestine in an exceedingly interesting fashion ; the surface of the mucosa is thickly studded with innumerable, fine, short projections resembling the pile of velvet. These are invested by surface epithelium, and amongst them, at their feet, open the before-mentioned *crypts of Lieberkühn.* They are the so-called *villi.* Each contains a lymphatic vessel, blood-vessels, and involuntary muscular fibres, all supported by adenoid connective tissue like that of the mucosa below ;

FIG. 24.



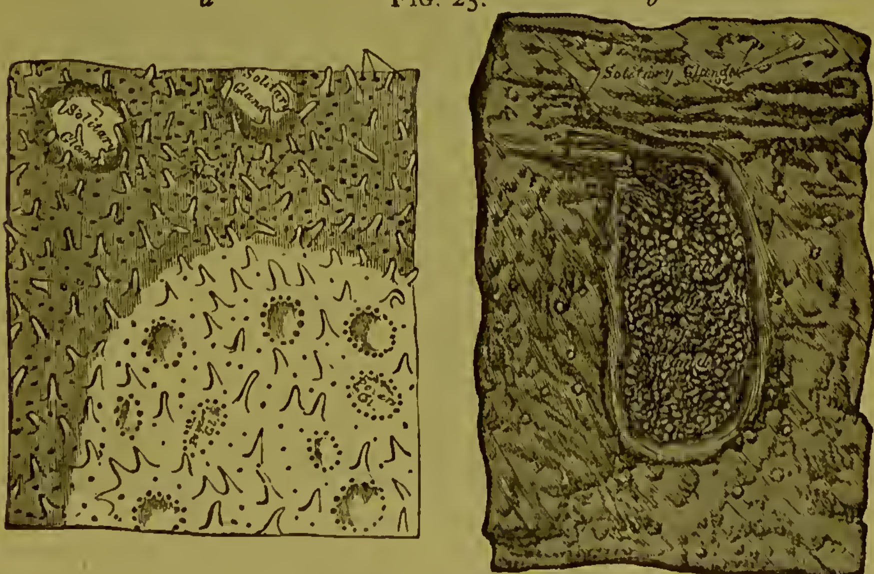
THE LACTEALS AND LYMPHATICS OF THE SMALL INTESTINE.
(QUAIN'S ANATOMY.)

the lymphatic is in the axis of the villus, the muscles form the next layer, and the blood-vessels lie immediately beneath the epithelium. When the muscular layer of the

villus contracts it must of necessity compress the lymph vessel, whilst causing no impediment to the flow of blood.

"We have described the mucous membrane of the stomach and intestines as containing a framework of adenoid reticular tissue like the tissue of lymphatic follicles. It is, indeed, identical with this,—a network of branched cells with oval nuclei, and the meshes of which are crowded with lymph corpuscles with round nuclei. At certain points in the intestines the adenoid tissue of the mucosa presents local nodular enlargements; the mucosa at these points becomes so much thicker that it swells up at the free surface beneath the epithelium into rounded eminences about as large as millet-seeds or the heads of small pins; and at the under surface of the mucosa it dips into the submucous tissue in a similar manner. At the base of this nodule of adenoid tissue in the submucosa there is usually a network of wide, thin-walled, lymphatic vessels. Many of these rounded masses are scattered irregularly over small and large intestines as the *solitary follicles* or *glands* (Fig. 25, *a*), but at the lower end of the ileum they form little colonies, often covering an area an inch or more in length, and they are situated

a FIG. 25. *b*



a SOLITARY GLAND WITH VILLI. *b* PEYER'S PATCHES.
(GRAY'S ANATOMY.)

at that part of the intestine which is remote from the

attachment of the mesentery. They then constitute the so-called *Peyer's patches* (Fig. 25, *b*).

Nodular adenoid masses are, however, not limited to the adenoid mucosa of the intestines.

The whole of the intestines, and the stomach as well, are sustained in the abdominal cavity by sheets of delicate membrane, formed by folds of peritoneum, and called, in the case of the intestinal portion of the tube, the *mesentery*.

FIG. 26.

THE LYMPHATICS OF THE BODY.

Lac. The lacteals opening into the *receptaculum chyli* (R.C.), whence passes the thoracic duct, which opens at T, at the junction of the left subclavian and jugular veins. (*Yeo's Physiology.*)

Between the layers of the mesentery run the vessels and

nerves for the supply of the bowel. In addition to blood-vessels there are numerous thin-walled lymphatic vessels called *lacteals*, which are fed by the rich network of lymphatic vessels of the mucosa and submucosa, and which run in the mesentery to the back of the abdominal cavity. Here they are collected into a large lymphatic reservoir, the *receptaculum chyli*, from which a duct, the *thoracic duct*, proceeds along the side of the vertebral column to open into the venous system at the junction of the subclavian and jugular veins on the left side of the neck. The lacteal and lymphatic vessels, whose course has been briefly sketched, are interrupted at many points by the presence of lymphatic glands. These may be simply regarded as labyrinthine systems of vessels into which the simple *afferent* lymphatic or lacteal vessels open, and each of which is surrounded and penetrated by adenoid connective tissue, like that of the intestinal mucosa. The lacteal vessels after food are filled with a milky fluid, the *chyle*. They were discovered by Aselli in the year 1662."

The part played by blood vessels and lymphatics in the absorption of the nutritive matters from the small intestine is not perfectly understood, though in all probability the following statement is true. The absorption of dissolved and diffusible matters, such as salts, sugars and peptones is carried on by the capillaries of the villi ; unquestionably during digestion both sugars and peptones are found in the blood coming from the small intestine. The emulsionized fats make their way, however, almost entering into the lacteals of the villi.

The lymphatics as a whole convey back to the blood the liquid which has transuded from the capillaries, and which has given up certain of its constituents to the anatomical elements of the tissues which it has bathed, whilst it has removed from them products of oxidation and waste, particularly CO_2. This liquid is called *Lymph*. The lymphatics of the alimentary canal, however, during digestion carry to the blood, lymph loaded with emulsioned fats, so that it is white as milk, and it is then called *Chyle;* this fluid is, as has been said, discharged into large veins near the heart.

The blood, we therefore see, is directly nourished with fatty matters absorbed from the intestine through the Chyle.

The Relations of the Liver to absorbed Matters.

If we exclude the fatty matters which, as I have told you, make their way chiefly into the lacteals and thence to the thoracic duct which conveys them into the blood, the substances absorbed into the intestine are mainly carried by the capillaries of the mucous membrane into the small venous radicles which pass into larger veins.

All the veins carrying blood back from the organs of digestion, and certain of their accessory organs, unite to form one larger vein, the Portal Vein or "Vena Portae." In the diagram now before us (Fig. 27) are shewn the chief branches which unite to form the Portal Vein. These veins bring the blood back from the stomach, spleen, pancreas, and gall-bladder, and from the small and large intestine. As will be seen by a reference to the diagram the greater number of the tributary branches of the portal vein unite first of all into two branches, termed the *splenic vein* and the *superior mesenteric vein*, and these joining behind the pancreas constitute the Vena Portæ, which after receiving veins from the stomach (*coronary veins*) enters the transverse fissure of the liver.

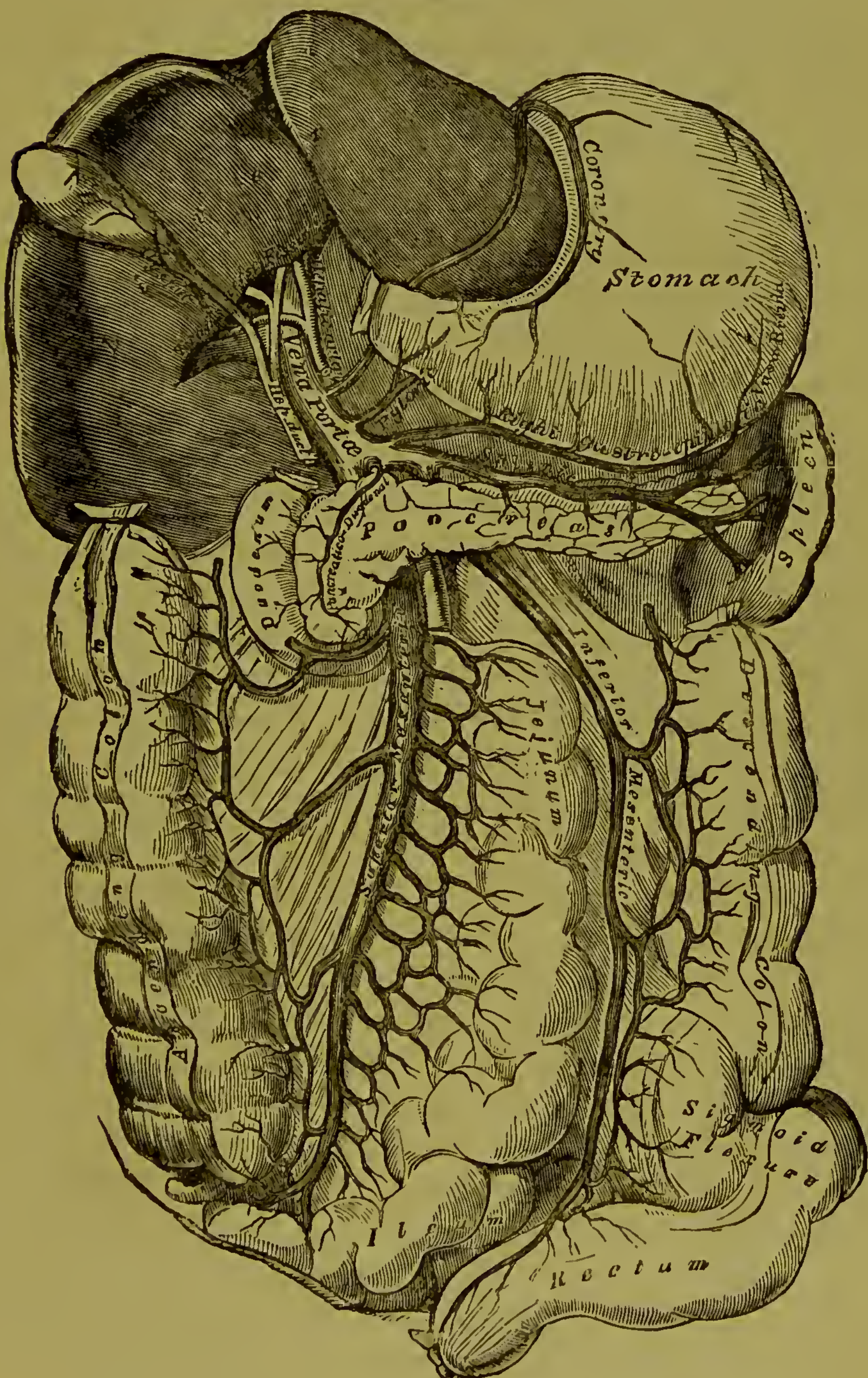
Venous blood is blood which has circulated through a capillary system, and in general is distinguished from the blood of arteries by its darker colour, by its smaller proportion of "respiratory" oxygen, and by its greater proportion of carbon dioxide. The blood of the portal vein differs from venous blood in general, however, in that after digestion, it contains the substances absorbed from the alimentary canal and the greater part of all the matters which are required to make up for the losses of the body—water, the products of "proteolytic" digestion, dextrins, and sugars.

Can we distinguish all the various constituents in portal blood, and in such amount as we might expect?

Unquestionably after digestion of a starchy or saccharine meal the portal venous blood does contain a larger quantity of sugar than the blood of any other vessel in the body.

Unquestionably, too, traces of peptones may be discovered by appropriate methods in such blood, though many have (through faulty methods) failed to discover them.

FIG. 27.



THE PORTAL VEIN AND ITS TRIBUTARIES. (GRAY'S ANATOMY.)

It is mainly owing to the observation of the second class of observers, that the view has come generally to be held, though it cannot be said to rest upon good evidence, that in the very act of passing from the intestines into the blood vessels, peptones are in part or wholly immediately reconverted into normal albuminous substances. This reconversion necessitates—if the views which I have explained to you on proteolysis be correct—an actual synthetic reconstruction of the molecule of albumin. Whether as dextrins or sugars, as peptones or reconstructed albumins, the main part of the proteids from the alimentary canal are, however, together with water, carried to the liver by the blood which flows along the portal vein.

In general, the veins of the body are formed by the union of capillary vessels, and joining with other veins, find their way into one or other of the great veins (the so-called *venae cavae superior et inferior*), which open into the right auricle. But the portal vein is the most striking exception to this common plan. Having entered the liver, it breaks up into innumerable small veins, which in their turn, form fine capillary meshworks. Amongst which are packed the myriads of secretory liver-cells. From these capillary systems there arise small veins which, uniting together, ultimately pass as so-called hepatic veins, and empty into the *vena cava inferior.*

What can the object be of having this immense gland the liver, in the path of the blood coming back from the digestive organs, charged with the products of digestion?

Before answering, in however brief and elementary a manner, this interesting question, let me point out that the blood which passes from the portal vein into its capillaries is circulating under a much lower pressure than the blood of capillary areas in general, and that in spite of certain facilities afforded by the nearness of the hepatic veins to the thorax, which exerts an aspirating influence upon the blood of the veins which enter it, the circulation through the liver substance must be an unusually slow one, as if to induce

a thorough action of the liver cells upon the matters transmitted from the portal blood.

Let me again point out to you that the blood which leaves the liver is much hotter than the blood which enters it; that the liver is the seat of the production of much heat, which of necessity is produced by the chemical actions going on within it, presumedly by the falling to pieces of more complex into more simple chemical compounds.

Having mentioned these facts, I may then inquire into some of the functions unquestionably exercised by the liver.

In the first place, when an animal is fed upon starches or sugars, we find that the liver stores up large quantities of "glycogen," a carbohydrate which has the same percentage composition, i.e., which is isomeric with the starches and dextrins, having the formula $(C_{12}\ H_{20}\ O_{10})_n$; this is a carbohydrate, doubtless of smaller molecular weight than the sugar from which the liver manufactures it. It is most readily converted into sugar.

When, therefore, the body receives large quantities of carbohydrates and sugars, instead of these passing as sugar directly from the alimentary canal into the blood, they are arrested by the liver, which stores them up as glycogen.

But what are the subsequent transformations of glycogen? you will ask. A question which I cannot satisfactorily answer.

When this matter was first enquired into by the great Claude Bernard, the simplest and most obvious explanation was given, based upon experimental evidence which has since, in the opinion of the most eminent scientific men, been found to be unreliable. The explanation was, that glycogen was as it were gradually paid out by the liver which had stored it, as grape sugar, which passing into the blood was there burned. This passage of sugar from the liver into the blood, which certainly occurs in the disease which we know as diabetes mellitus, does not occur in health. What then becomes of glycogen? It doubtless passes away from the liver in forms which as yet have escaped our detection, and in all

probability is carried chiefly to the muscular system, which it supplies with much of the non-nitrogenous organic matter which is continually being oxidized there.

I have followed very briefly the carbohydrates of the body and told you what influence the liver exerts upon them. Now it remains to enquire what becomes of the proteid matters which enter the liver, and to the questions which arise on this matter I am forced to give much more indefinite answers, if answers they can be called.

You know that as a result of the act of living there is a continual destruction of the proteid constituents which are an essential substratum of the protoplasmic framework of the body. The proteids yield mainly, as products of decomposition, carbonic acid, water, urea and sulphur compounds, of which some are oxidized completely, yielding their sulphur as sulphuric acid, and others pass away in small quantities from the body in the form of such bodies as taurine. To make up for this essential waste of proteids, we must take proteids as essential constituents of our diet.

What becomes of the peptones absorbed from the alimentary canal? Do they all in the first instance become reconverted into normal proteids, and do these proteids all become first of all part and parcel of the tissues of the body, and afterwards undergo "regressive metamorphosis?" Or is it likely that whilst some proteids follow the course hinted at in the hypothesis just enunciated, others undergo, almost as soon as they have entered the organism, a decomposition into simpler bodies, which are burned up and yield a part at least of the energy which the organism requires.

In all probability the course of events differs much according to the amount of proteid supplied to the economy, though both hypotheses are in part correct.

Without entering into the grounds for my assertions, I may say that, *sooner* or *later*, a decomposition of proteids occurs in the body, and that amongst the products formed are, firstly, fats, and, secondly, nitrogenous bodies, which ultimately in great part yield urea (CH_4N_2O).

Whilst decomposition of proteids probably has its seat to a small extent, wherever living protoplasm exists, evidence appears to point to the liver as the seat of the chief decomposition of proteids. The decomposition of proteids has not, however, a constant value for the same organism, but is conditioned by the nature of the diet of which the proteids form a part, and the mechanical work which the organism has to perform. If the proteid diet be largely in excess of the needs of the body, *i.e.*, more than sufficient to supply all its matter, and yield all its energy, then the fat which results from the proteid decomposition is stored up in the tissues, and may constitute a store of *reserve material* analogous to liver-glycogen ; if the diet be only adequate the fat is burned and not stored.

By giving starchy and especially fatty food, the proteids are shielded in great measure from decomposition, and the fat which results from the transformation of proteids is stored up and the animal fattens. In the end, however, all the organic constituents which have been introduced into the body are oxidized. This oxidation, which is effected through the agency of the oxygen originally derived from the air which has become linked to the blood-colouring matter, does not take place in the blood, but as a result of the living operations of the protoplasmic elements of all tissues and organs.